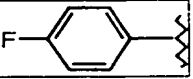
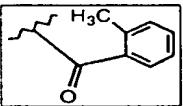
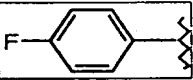
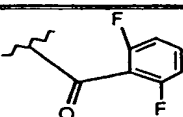
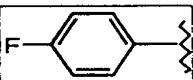
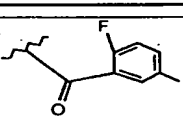

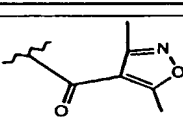
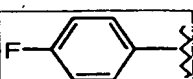
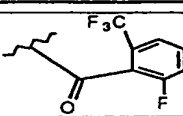
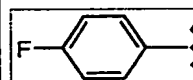
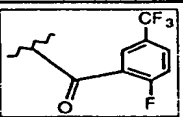
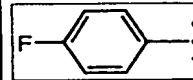
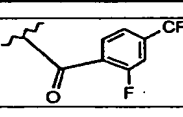
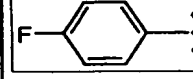
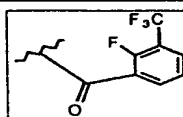
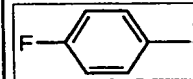
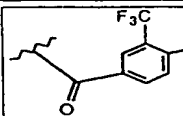
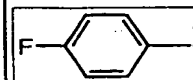
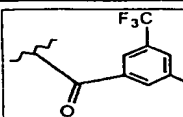
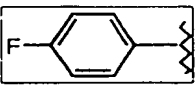
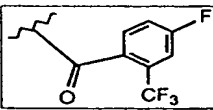
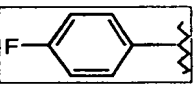
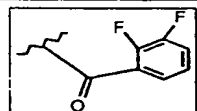
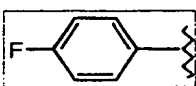
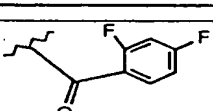
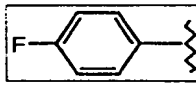
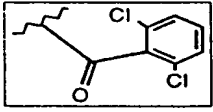
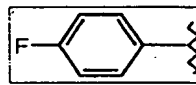
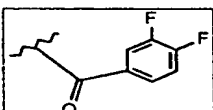
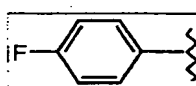
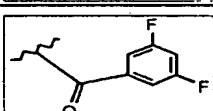
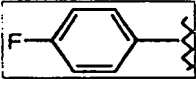
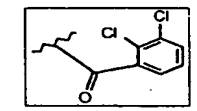
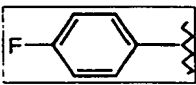
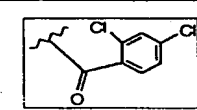
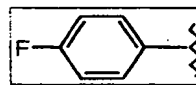
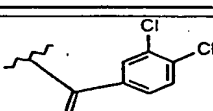
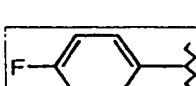
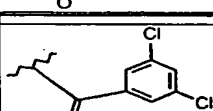


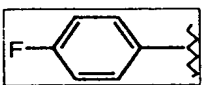
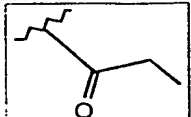
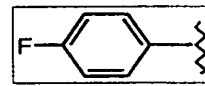
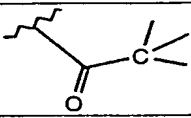
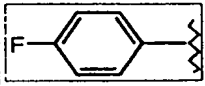
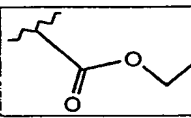
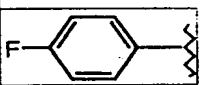
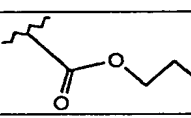
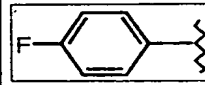
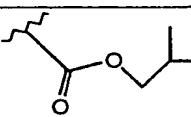
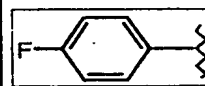
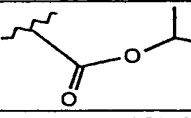
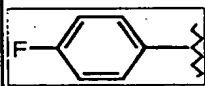
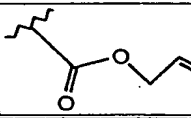
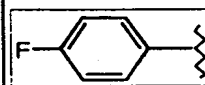
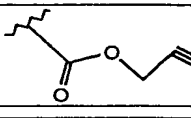
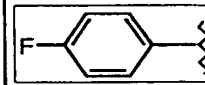
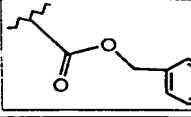
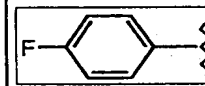
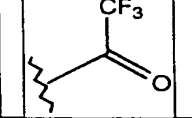
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1400			74	440	441
B-1401			76	462	463
B-1402			65	462	463
B-1403			64	445	446
B-1404			70	512	513
B-1405			57	512	513
B-1406			73	512	513
B-1407			80	512	513
B-1408			2	512	513
B-1409			62	512	513

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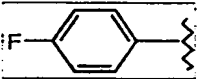
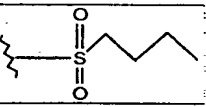
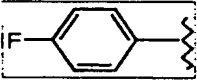
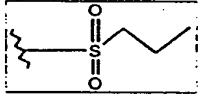
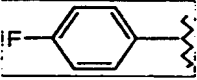
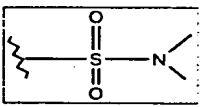
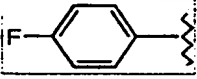
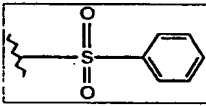
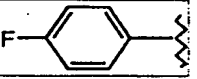
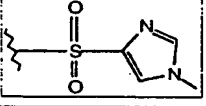
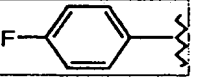
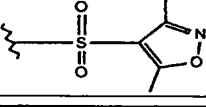
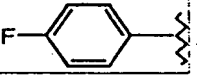
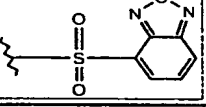
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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1410			42	512	513
B-1411			19	462	463
B-1412			74	462	463
B-1413			75	494	495
B-1414			68	462	463
B-1415			48	462	463
B-1416			48	494	495
B-1417			57	494	495
B-1418			49	494	495
B-1419			39	494	495

SUBSTITUTESHEET (RULE 26)

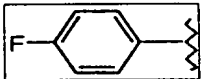
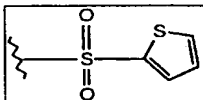
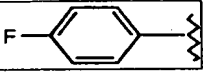
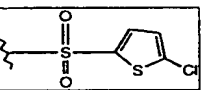

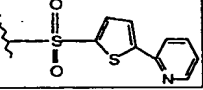
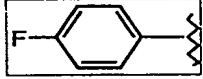
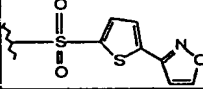

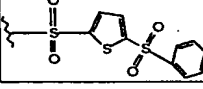
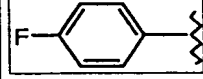
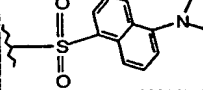
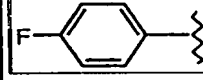
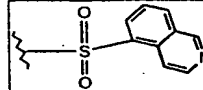
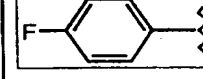
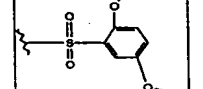
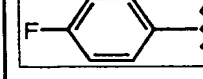
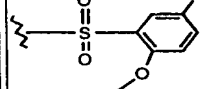
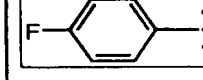
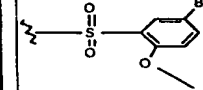
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1420			72	378	379
B-1421			74	406	407
B-1422			68	394	395
B-1423			57	408	409
B-1424			77	422	423
B-1425			26	408	409
B-1426			41	406	407
B-1427			37	404	405
B-1428			60	456	457
B-1429			2	418	419


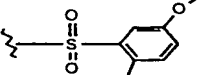
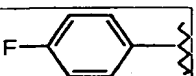
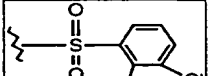
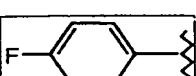
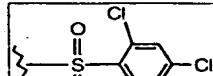
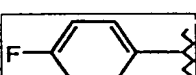
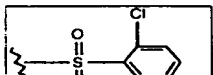
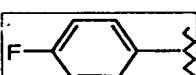
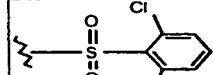
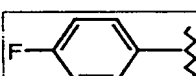
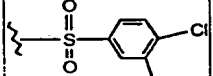
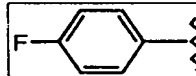
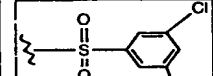
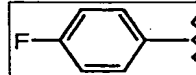
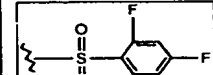
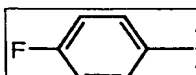
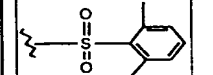
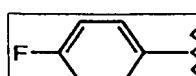
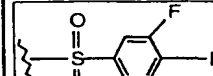
SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1430			61	442	443
B-1431			64	428	429
B-1432			71	429	430
B-1433			74	462	463
B-1434			88	466	467
B-1435			75	481	482
B-1436			71	504	505

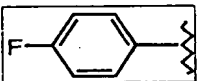
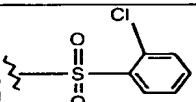
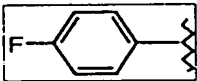
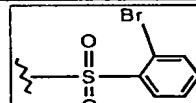
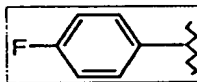
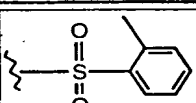
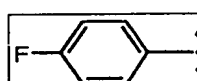
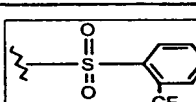
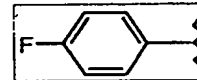
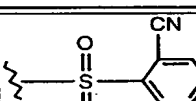
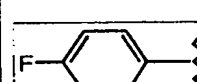
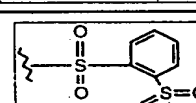
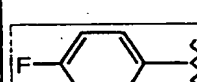
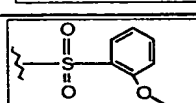
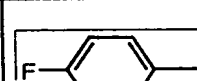
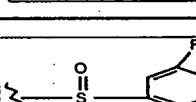
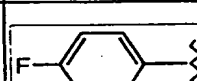
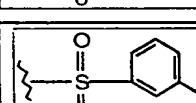
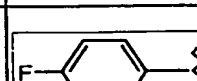
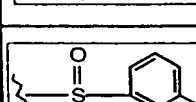
SUBSTITUTE SHEET (RULE 26)



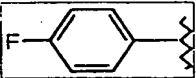
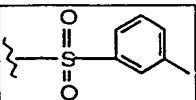
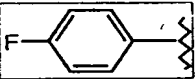
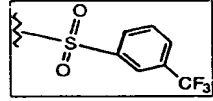
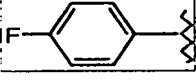
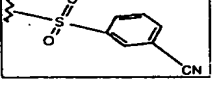
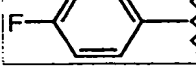
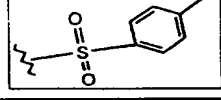
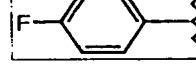
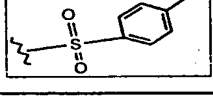
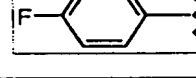
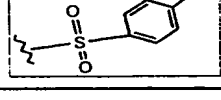
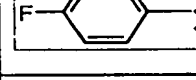
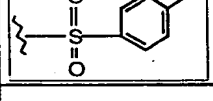
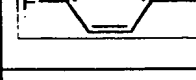
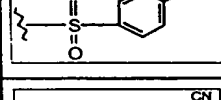

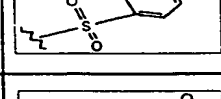
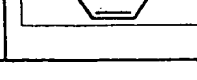
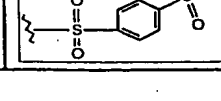
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1437			63	468	469
B-1438			78	502	503
B-1439			70	545	546
B-1440			62	535	536
B-1441			82	608	
B-1442			79	555	556
B-1443			28	513	514
B-1444			75	522	523
B-1445			74	526	527
B-1446			70	570	571

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1447			73	506	507
B-1448			76	530	531
B-1449			82	530	531
B-1450			83	530	531
B-1451			74	530	531
B-1452			76	530	531
B-1453			73	530	531
B-1454			81	498	499
B-1455			83	498	499
B-1456			78	498	499

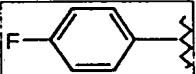
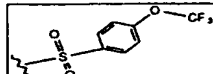
SUBSTITUTESHEET (RULE 26)


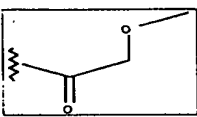
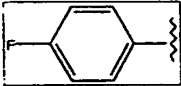
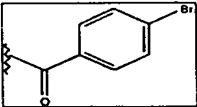
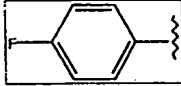
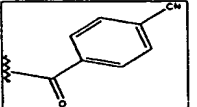
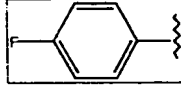
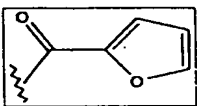
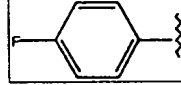
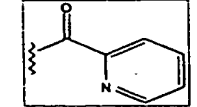

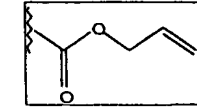
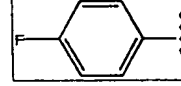
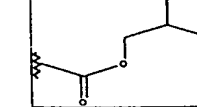
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1457			74	496	497
B-1458			82	540	541
B-1459			80	476	477
B-1460			78	530	531
B-1461			82	487	488
B-1462			71	540	541
B-1463			78	546	547
B-1464			83	480	481
B-1465			84	496	497
B-1466			80	540	541

SUBSTITUTE SHEET (RULE 26)

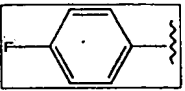
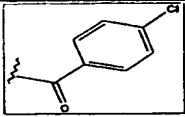
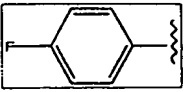
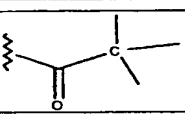
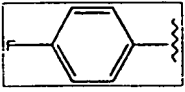
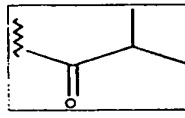

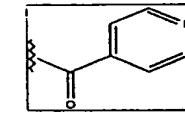

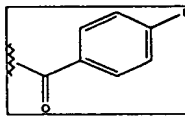

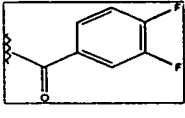
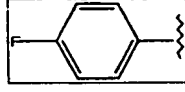
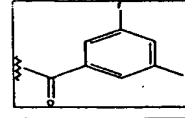
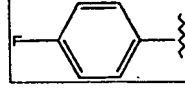
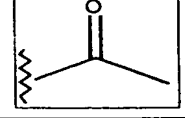
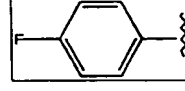
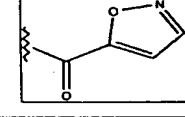

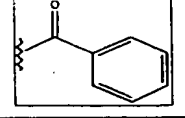
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1467			79	476	477
B-1468			79	530	531
B-1469			75	487	488
B-1470			80	480	481
B-1471			74	496	497
B-1472			75	540	541
B-1473			77	476	477
B-1474			81	530	531
B-1475			70	487	488
B-1476			54	540	541

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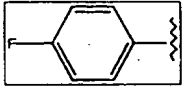
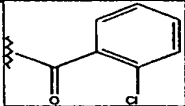
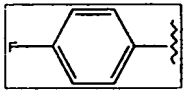
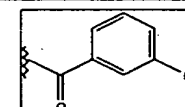

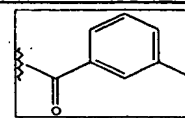
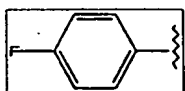
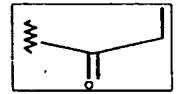
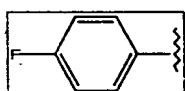
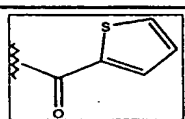
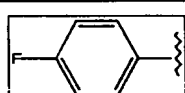
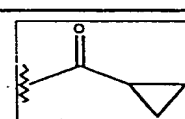

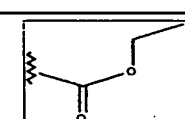

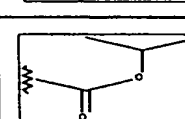

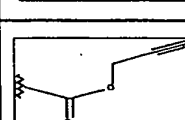
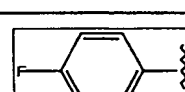
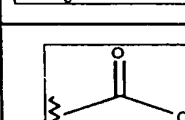
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1477			79	546	547

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1478			87	394	395
B-1479			41	504	505
B-1480			87	451	452
B-1481			18	416	417
B-1482			77	427	428
B-1483			74	406	407
B-1484			82	422	423

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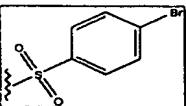

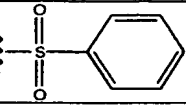
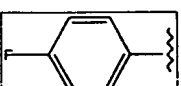
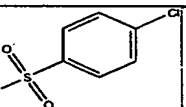
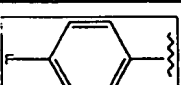
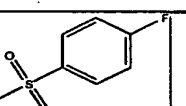
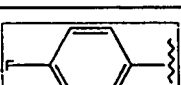
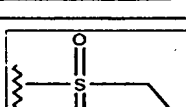
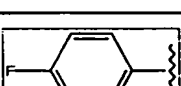
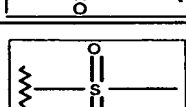
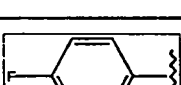
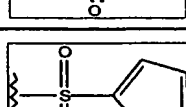



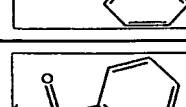

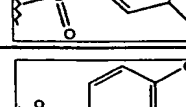
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1485			85	460	461
B-1486			64	406	407
B-1487			71	392	393
B-1488			82	427	428
B-1489			87	444	445
B-1490			81	462	463
B-1491			87	462	463
B-1492			69	364	365
B-1493			53	417	418
B-1494			17	426	427

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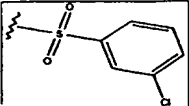

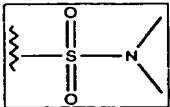
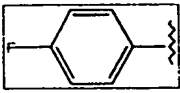
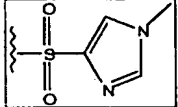
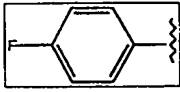
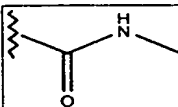
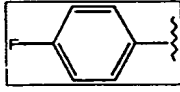
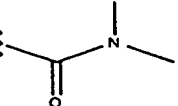
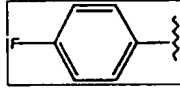
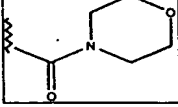

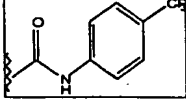
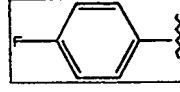
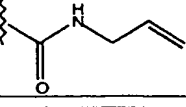
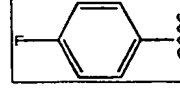
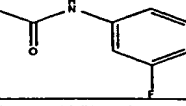
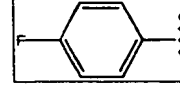
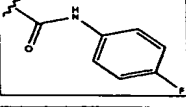
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1495			79	460	461
B-1496			80	444	445
B-1497			82	460	461
B-1498			72	378	379
B-1499			70	432	433
B-1500			68	390	391
B-1501			63	394	395
B-1502			78	408	409
B-1503			55	404	405
B-1504			39	418	419

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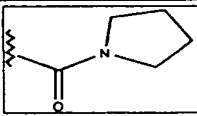
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1505			69	540	541
B-1506			69	462	463
B-1507			70	496	497
B-1508			65	480	481
B-1509			56	414	415
B-1510			62	400	401
B-1511			30	468	469
B-1512			50	476	477
B-1513			44	540	541
B-1514			42	530	531

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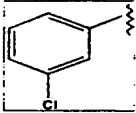
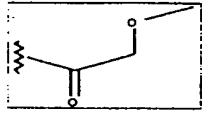
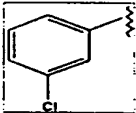
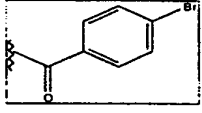
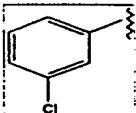
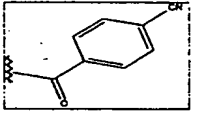
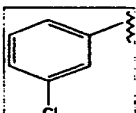
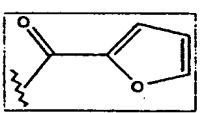
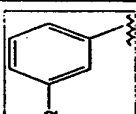
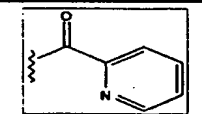
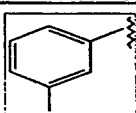
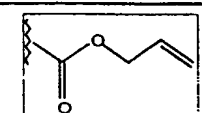
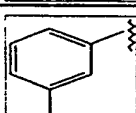
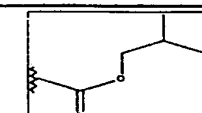
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1515			68	496	497
B-1516			27	429	430
B-1517			92	466	467
B-1518			33	379	380
B-1519			50	393	394
B-1520			82	435	436
B-1521			86	509	510
B-1522			12	405	406
B-1523			59	459	460
B-1524			81	459	460

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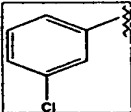
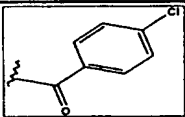
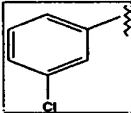
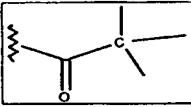
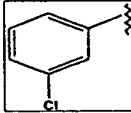
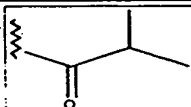
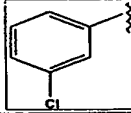
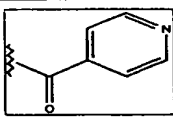
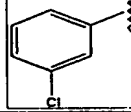
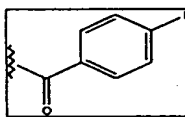
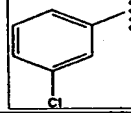
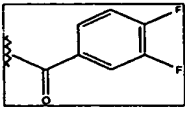
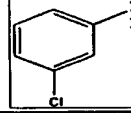
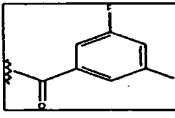
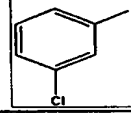
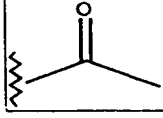
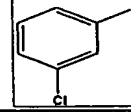
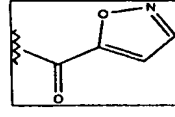
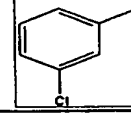
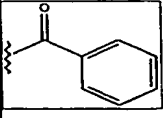
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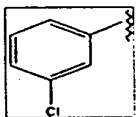
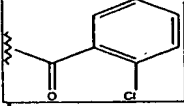
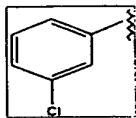
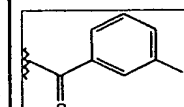
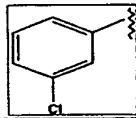
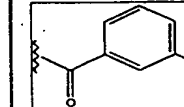
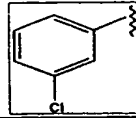
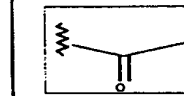
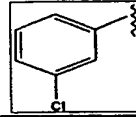
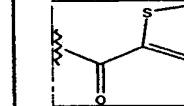
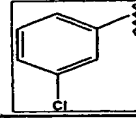
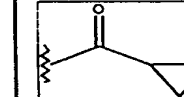
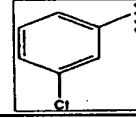
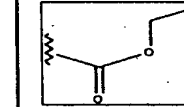
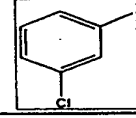
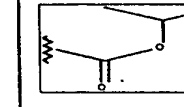
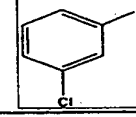
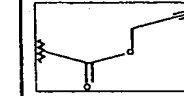
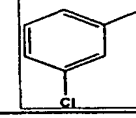
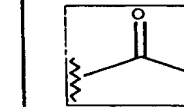
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1525			57	419	420

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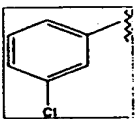
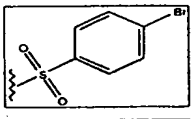
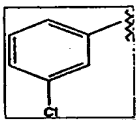
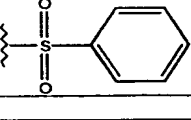
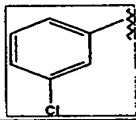
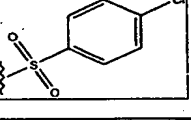
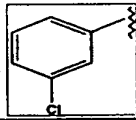
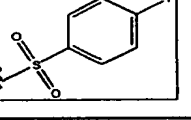
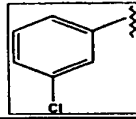
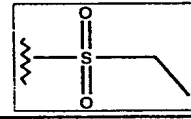
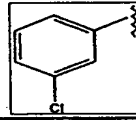
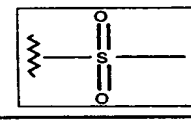
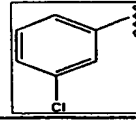
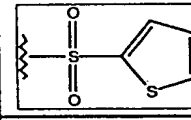
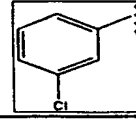
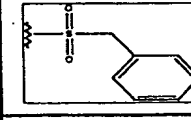
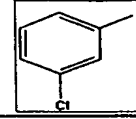
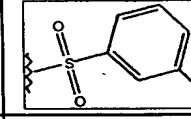
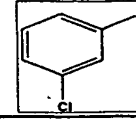
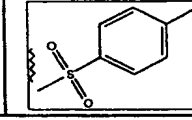
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1526			73	410	411
B-1527			66	520	521
B-1528			91	467	468
B-1529			73	432	433
B-1530			91	443	444
B-1531			74	422	423
B-1532			68	438	439

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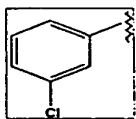
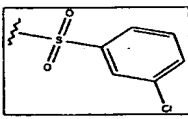
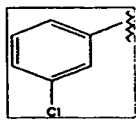
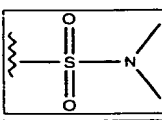
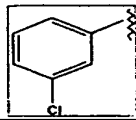
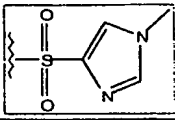
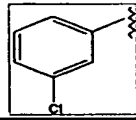
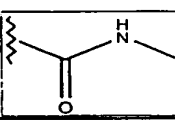
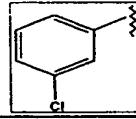
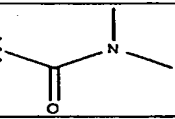
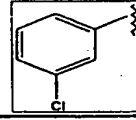
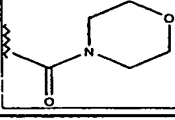
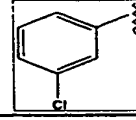
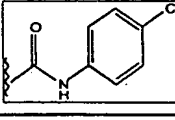
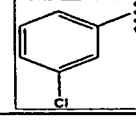
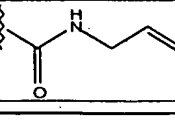
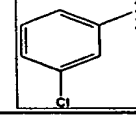
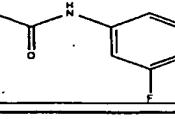
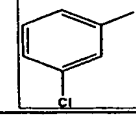
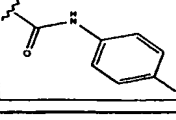
Example#	R <sup>2</sup>	R <sup>1</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1533			84	476	477
B-1534			72	422	423
B-1535			78	408	409
B-1536			77	443	444
B-1537			86	460	461
B-1538			74	478	479
B-1539			85	478	479
B-1540			71	380	381
B-1541			71	433	434
B-1542			89	442	443

Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1543			82	476	477
B-1544			76	460	461
B-1545			77	476	477
B-1546			76	394	395
B-1547			58	448	449
B-1548			83	406	407
B-1549			67	410	411
B-1550			37	424	425
B-1551			55	420	421
B-1552			23	434	435

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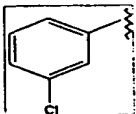
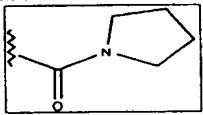
Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1553			83	556	557
B-1554			84	478	479
B-1555			93	512	513
B-1556			83	496	497
B-1557			62	430	431
B-1558			45	416	417
B-1559			67	484	485
B-1560			16	492	493
B-1561			84	556	557
B-1562			74	546	547

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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1563			72	512	513
B-1564			57	445	446
B-1565			64	482	483
B-1566			71	395	396
B-1567			54	409	410
B-1568			76	451	452
B-1569			70	525	526
B-1570			79	421	422
B-1571			60	475	476
B-1572			77	475	476



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Example#	R <sup>2</sup>	R <sup>L</sup>	%Yield	Calcd. Mass Spec	Observed Mass Spec (M+H)
B-1573			65	435	436

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Proton NMR data for selected members from Examples B-0001 through B-1573 are shown in the following table.

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Plate ID	<sup>1</sup> H NMR(solvent), $\delta$ ppm
B-0120	(DMF-d7) $\delta$ 8.53(bd, J = 4.99Hz, 2H), 7.44-7.24(m, 11H), 4.41(s, 2H), 4.31(br, 2H)
B-0224	(DMF-d7) $\delta$ 8.56(bd, J = 4.98Hz, 2H), 7.78-7.69(m, 4H), 7.39-7.19(m, 6H), 4.23(br, 2H)
B-0235	(DMF-d7) $\delta$ 8.47(br, 2H), 7.91-7.75(m, 3H), 7.57-7.53(m, 1H), 7.38-7.34(m, 2H), 7.21-7.13(m, 4H), 4.20(br, 2H)
B-0244	(CDCl <sub>3</sub> /CD <sub>3</sub> OD) $\delta$ 8.38(d, J = 5.38 Hz, 1H), 7.62-7.32(m, 9H), 7.04-6.95(m, 4H), 6.86-6.80(m, 2H), 4.52(q, J = 6.96 Hz, 1H), 1.40(d, J = 6.88 Hz, 3H)
B-0256	(DMF-d7) $\delta$ 8.45(bd, J = 2.85, 2H), 7.87(br s, 4H), 7.76-7.75(m, 2H), 7.53-7.33(m, 5H), 7.18-7.13(br, 4H)
B-0426	(DMF-d7), 1.32(br, 3H), 1.67(br, 3H), 4.17(br, 2H), 5.12(br, 1H), 7.50(m, 6H), 8.77(m, 2H), 13.54(br, 1H).
B-0438	(DMSO), 1.14(t, J = 6.9 Hz, 3H), 4.54(m, 1H), 6.99(br, 2H), 7.21(br, 4H), 7.45(s, 1H), 7.61(q, J = 8.7 Hz, 2H), 8.52(d, J = 5.2 Hz, 2H).
B-0466	(DMF-d7), 1.61(brd, J = 30.6 Hz, 3H), 4.61 (br, 1H), 7.25(m, 6H), 7.65(m, 3H), 8.59(br, 2H), 13.34(brd, J = 34.8 Hz, 1H).
B-0473	(CD <sub>3</sub> OD), 1.53(d, J = 7.2 Hz, 3H), 4.59(q, J = 7.2 Hz, 1H), 6.88(d, J = 4 Hz, 1H), 7.09(m, 3H), 7.15(dd, J = 4.4, 1.6 Hz, 2H), 7.26(m, 2H), 8.46(d, J = 6.0 Hz, 2H).
B-0477	(DMF), 1.80(br, 3H), 2.35(s, 1H), 4.98(br, 1H), 7.38(m, 6H), 7.85(m, 2H), 8.45(br, 1H), 8.75(d, J = 6.0 Hz, 2H).
B-0479	(Methanol-d <sub>4</sub> ), 1.57(d, J = 5.6 Hz, 3H), 4.74(br, 1H), 7.23(m, 4H), 7.60(m, 2H), 7.81(m, 4H), 8.67(br, 2H).
B-0487	(DMF), 1.78(s, 3H), 2.76(br, 6H), 4.85(br, 1H), 7.42(br, 2H), 7.54(br, 2H), 7.66(br, 3H), 8.82(s, 2H).
B-0566	(CD <sub>3</sub> OD), 1.38(d, J = 7.2 Hz, 3H), 4.15(br, 2H), 4.50(br, 1H), 7.04(br, 2H), 7.18(br, 2H), 7.30(m, 7H), 8.45(m, 2H).
B-0569	(CD <sub>3</sub> OD), 1.56(br, 3H), 4.66(q, J = 6.7 Hz, 1H), 7.17(m, 8H), 7.56(m, 2H), 8.47(s, 2H).
B-0574	(Methanol-d <sub>4</sub> ), 1.49(br, 3H), 3.86(br, 3H), 4.60(br, 1H), 6.92(br, 2H), 7.19(br, 2H), 7.31(br, 2H), 7.76(m, 4H), 8.60(br, 2H).
B-0639	(DMF-d7), 1.58(brd, J = 30.0 Hz, 3H), 4.62(br, 1H), 7.25(m, 6H), 7.60(m, 4H), 8.59(br, 2H), 13.30(brd, J = 12.3 Hz).
B-0643	7.18(m, 2H), 7.32(dd, J = 6.0, 4.4 Hz, 1H), 7.70(dd, J = 9.0, 5.8Hz, 1H), 8.43(dd, J = 4.8, 3.2 Hz, 2H).
B-0650	(CD <sub>3</sub> OD), 1.58(br, 3H), 4.62(q, J = 6.6 Hz, 1H), 6.93(br, 1H), 7.17(m, 5H), 7.31(br, 2H), 8.51(br, 2H).
B-0656	(CDCl <sub>3</sub> /CD <sub>3</sub> OD) $\delta$ 8.48 (d, J = 5.30 Hz, 2H), 7.72-7.59(m, 4H), 7.14-7.10(m, 2H), 7.03-6.97(m, 4H), 4.60(q, J = 7.57Hz, 1H), 1.43(d, J = 7.26Hz, 3H)
B-0663	(CD <sub>3</sub> OD), 1.52(d, J = 6.8 Hz, 3H), 3.75(s, 3H), 7.21(m, 2H), 7.42(m, 2H), 7.57(s, 1H), 7.76(s, 1H), 7.98(br, 2H), 8.76(br, 2H).
B-1165	Hz, 2H), 3.06(m, 1H), 3.43(q, J = 6.1 Hz, 2H), 7.02(m, 2H), 7.14(m, 2H), 7.41(m, 2H), 8.59(d, J = 5.6 Hz, 2H).
B-1169	= 1.6 Hz, 1H), 7.04(t, J = 8.6 Hz, 2H), 7.14(m, 2H), 7.36(m, 2H), 8.39(d, J = 1.8 Hz, 1H), 8.60(m, 2H).
B-1171	6.83(br, 1H), 7.02(t, J = 8.7 Hz, 2H), 7.15(d, J = 5.6 Hz, 2H), 7.40(m, 2H), 8.59(d, J = 5.0 Hz, 2H).

Plate ID	<sup>1</sup> H NMR(solvent), $\delta$ ppm
B-1179	(CDCl <sub>3</sub> ), 1.94(br, 2H), 2.53(s, 3H), 2.85(t, J = 6.2 Hz, 2H), 3.65(br, 2H), 6.15(br, 1H), 7.04(m, 3H), 7.22(m, 3H), 7.41(br, 4H), 8.60(br, 2H).
B-1183	(CDCl <sub>3</sub> ), 2.00(br, 2H), 2.85(br, 2H), 3.64(br, 2H), 7.03(br, 3H), 7.17(br, 2H), 7.36(br, 2H), 7.66(br, 2H), 8.60(br, 2H), 8.77(br, 2H).
B-1194	(DMSO), 1.76(br, 2H), 2.66(br, 2H), 2.91(br, 2H), 4.30(s, 2H), 7.18(br, 5H), 7.35(m, 6H), 8.54(d, J = 5.8 Hz, 2H).
B-1200	(DMSO), 1.17(br, 3H), 1.76(br, 2H), 2.71(br, 2H), 2.97(br, 4H), 7.18(br, 4H), 7.36(br, 2H), 8.54(br, 2H).
B-1206	(DMSO), 1.03(s, 6H), 1.68(br, 2H), 2.63(br, 2H), 3.00(br, 2H), 3.65(br, 1H), 5.69(m, 2H), 7.16(br, 4H), 7.35(br, 2H), 8.54(br, 2H).
B-1216	(DMSO), 1.75(m, 2H), 2.14(s, 6H), 2.66(br, 2H), 3.10(br, 2H), 7.04(br, 3H), 7.18(br, 4H), 7.35(m, 2H), 7.47(br, 1H), 8.54(d, J = 4.8 Hz, 2H).
B-1226	(DMF), 1.25(br, 3H), 2.01(br, 2H), 3.35(br, 4H), 6.20(s, 1H), 6.30(s, 1H), 7.42(br, 4H), 7.65(br, 2H), 8.77(s, 2H).
B-1360	(DMSO-d <sub>6</sub> ), 1.80(br, 4H), 2.82(br, 1H), 2.94(br, 1H), 3.10(br, 1H), 3.60(br, 1H), 4.54(br, 1H), 7.18(m, 4H), 7.30(m, 4H), 7.46(m, 2H), 8.54(br, 2H).
B-1361	(DMSO-d <sub>6</sub> ), 0.99(br, 6H), 1.73(br, 4H), 2.89(br, 2H), 3.03(m, 1H), 4.04(br, 2H), 4.44(m, 1H), 7.18(m, 4H), 7.30(m, 2H), 8.57(d, J = 4.64 Hz, 2H).
B-1363	(DMSO-d <sub>6</sub> ), 1.78(br, 4H), 2.01(s, 3H), 2.89(br, 1H), 3.05(br, 1H), 3.34(br, 1H), 3.85(br, 1H), 4.48(br, 1H), 7.12(br, 2H), 7.21(br, 2H), 7.30(br, 2H), 8.69(br, 2H).
B-1364	(CDCl <sub>3</sub> ), 0.78(dd, J = 3.0, 2.9 Hz, 2H), 1.00(s, 2H), 1.78(m, 1H), 1.86(b, 4H), 2.64(m, 1H), 2.99(m, 1H), 3.16(m, 1H), 4.33(br, 1H), 4.70(br, 1H), 6.99(m, 2H), 7.14(s, 2H), 7.29(m, 2H), 8.64(s, 2H).
B-1368	(CDCl <sub>3</sub> ), 1.89(s, 4H), 2.65(m, 1H), 2.96(m, 1H), 3.06(m, 1H), 3.43(s, 3H), 3.93(d, J = 13.2 Hz, 1H), 4.09(d, J = 13.5 Hz, 1H), 4.18(d, J = 13.5 Hz, 1H), 4.68(d, J = 12.4 Hz, 1H), 7.60(m, 2H), 7.12(s, 2H), 7.26(m, 2H), 8.63(s, 2H).

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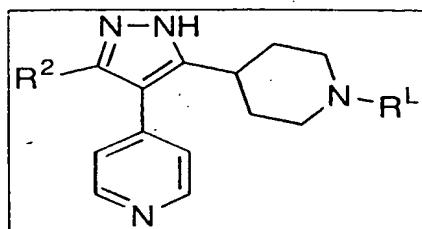
By analogy to the procedure identified above for the  
preparation of Examples B0001-B0048, the following  
15 examples B-1574 through B-2269 are prepared.

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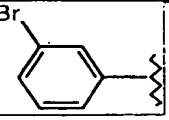
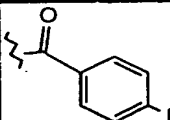
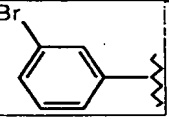
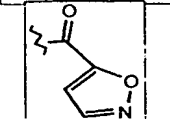
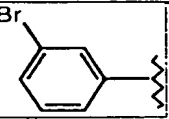
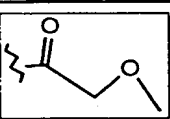
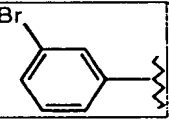
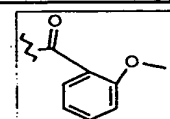
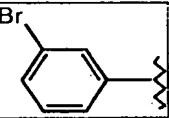
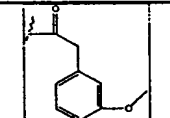
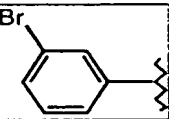
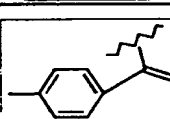
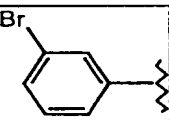
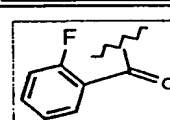
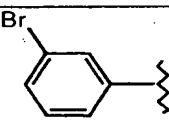
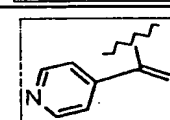
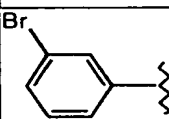
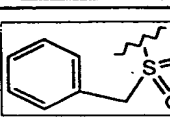
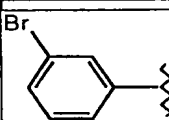
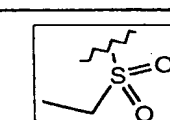
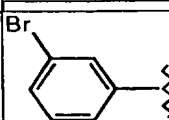
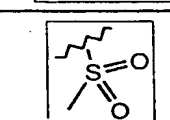
Examples B-1574 through B-1597 are prepared from Scaffold C-27

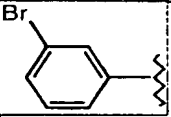
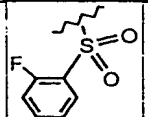
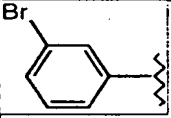
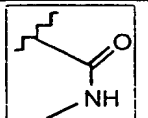
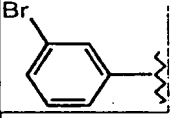
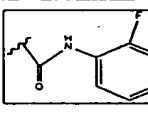
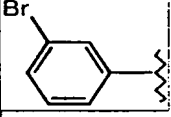
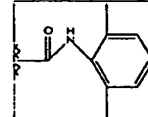
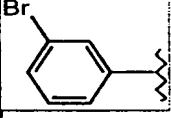
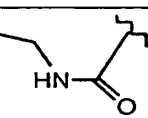
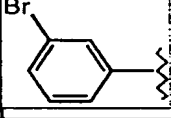
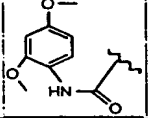
Example#

R<sup>2</sup>R<sup>L</sup>

B-1574					
B-1575					
B-1576					
B-1577					
B-1578					
B-1579					
B-1580					

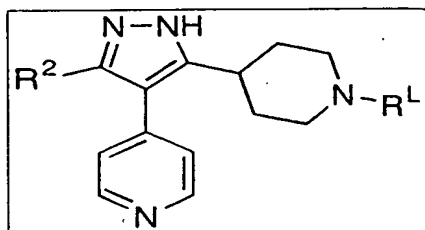
SUBSTITUTE SHEET (RULE 26)

B-1581					
B-1582					
B-1583					
B-1584					
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B-1597					



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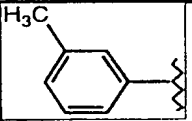
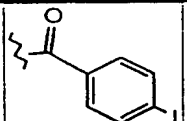
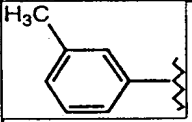
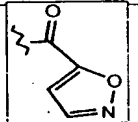
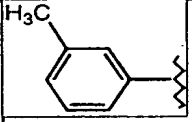
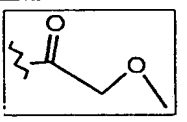
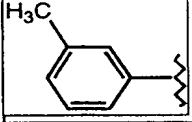
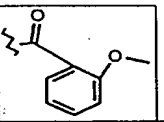
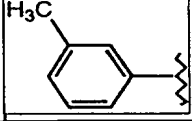
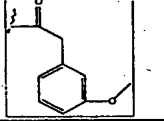
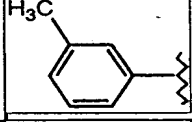
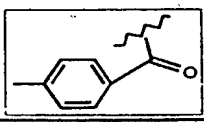
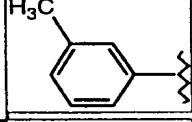
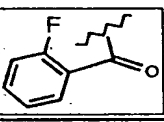
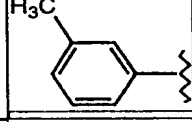
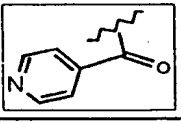
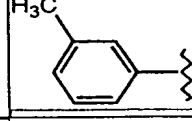
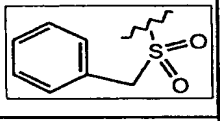
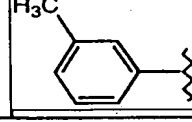
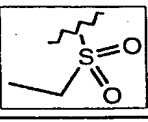
Examples B-1598 through B-1621 are prepared from Scaffold C-28

Example#

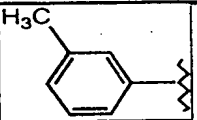
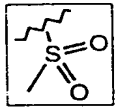
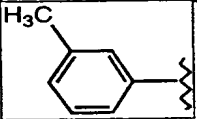
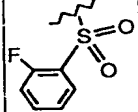
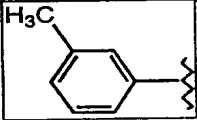
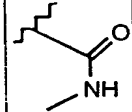
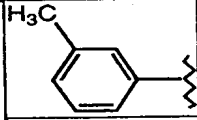
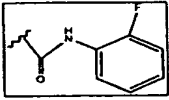
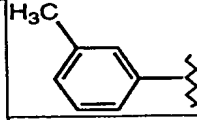
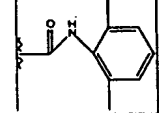
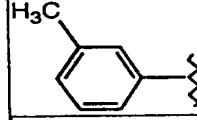
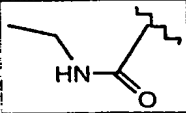
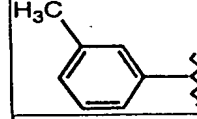
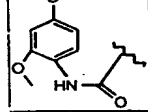
 $R^2$  $R^L$ 

B-1598					
B-1599					
B-1600					
B-1601					
B-1602					
B-1603					
B-1604					

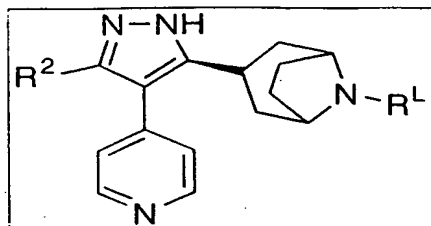
SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1605					
B-1606					
B-1607					
B-1608					
B-1609					
B-1610					
B-1611					
B-1612					
B-1613					
B-1614					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1615					
B-1616					
B-1617					
B-1618					
B-1619					
B-1620					
B-1621					

532



Examples B-1622 through B-1645 are prepared from Scaffold C-38

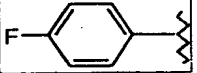
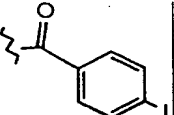
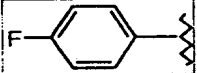
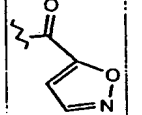
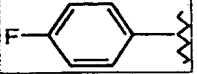
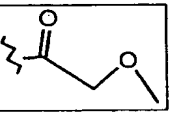
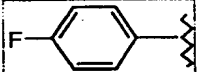
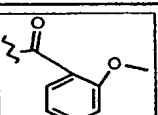

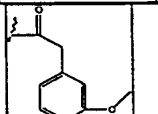
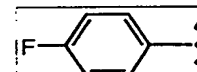
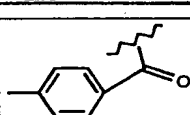
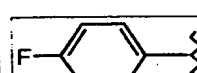
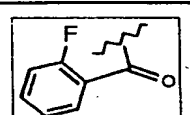
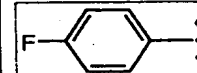
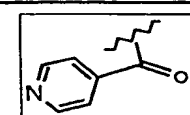
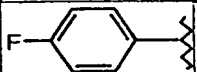
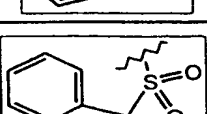
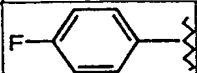
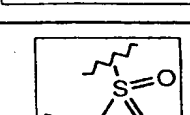
Example#

R²

R¹

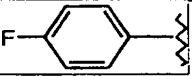
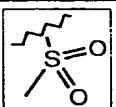
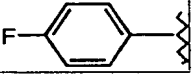
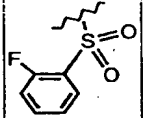
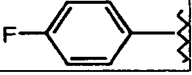
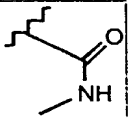
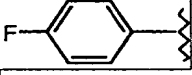
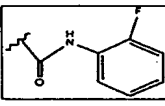
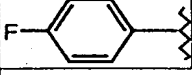
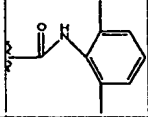
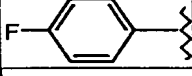
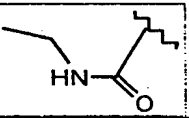
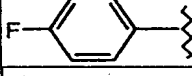
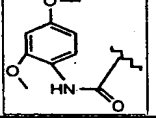
B-1622					
B-1623					
B-1624					
B-1625					
B-1626					
B-1627					
B-1628					

SUBSTITUTE SHEET (RULE 26)

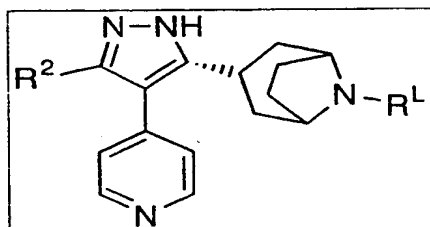
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1629					
B-1630					
B-1631					
B-1632					
B-1633					
B-1634					
B-1635					
B-1636					
B-1637					
B-1638					

Example#

 $R^2$  $R^L$ 

B-1639					
B-1640					
B-1641					
B-1642					
B-1643					
B-1644					
B-1645					

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Examples B-1646 through B-1669 are prepared from Scaffold C-39

Example#

R²

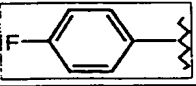
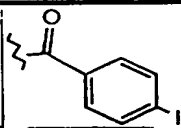
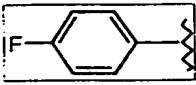
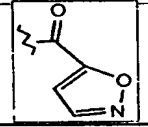
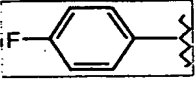
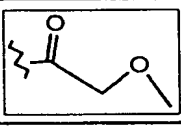
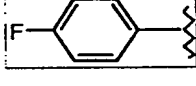
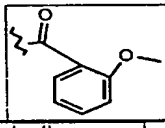
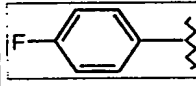
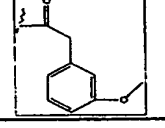
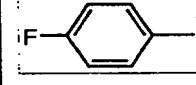
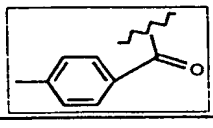
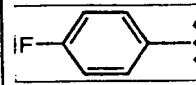
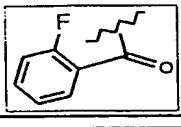
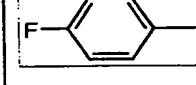
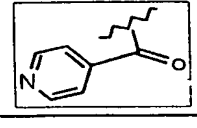
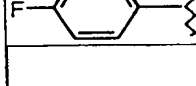
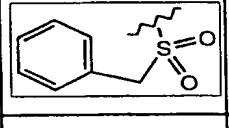
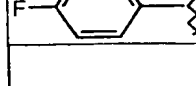
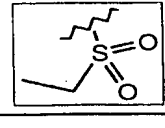
R¹

B-1646					
B-1647					
B-1648					
B-1649					
B-1650					
B-1651					
B-1652					

SUBSTITUTE SHEET (RULE 26)

Example#

 $R^2$  $R^L$ 

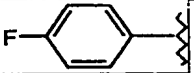
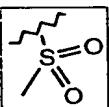

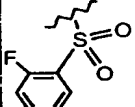

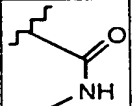

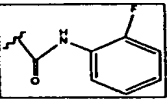
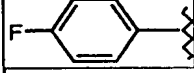
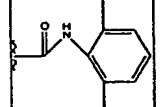

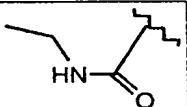
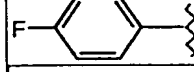
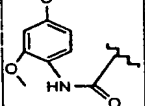
B-1653					
B-1654					
B-1655					
B-1656					
B-1657					
B-1658					
B-1659					
B-1660					
B-1661					
B-1662					

SUBSTITUTE SHEET (RULE 26)



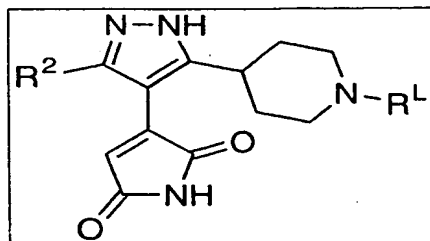
Example#

 $R^2$  $R^L$ 

B-1663					
B-1664					
B-1665					
B-1666					
B-1667					
B-1668					
B-1669					

SUBSTITUTE SHEET (RULE 26)

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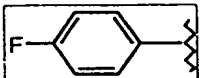
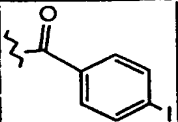
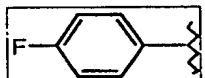
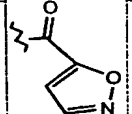
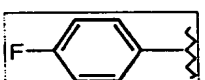
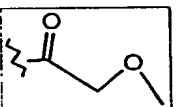
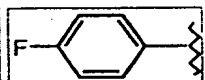
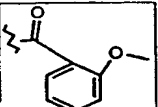
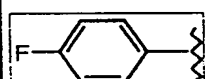
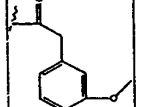
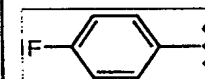
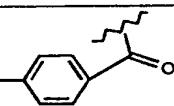
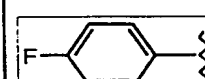
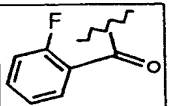
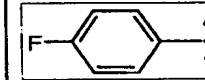
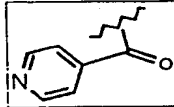
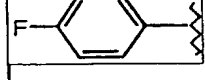
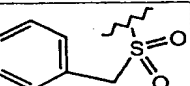
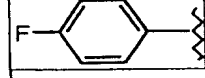
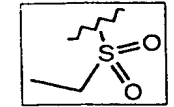
Examples B-1670 through B-1693 are prepared from Scaffold C-65

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1670					
B-1671					
B-1672					
B-1673					
B-1674					
B-1675					
B-1676					

SUBSTITUTESHEET (RULE 26)

Example#

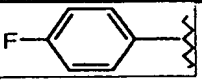
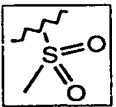
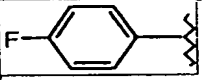
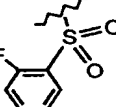
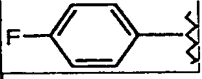
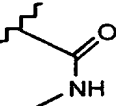
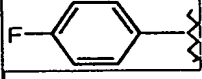
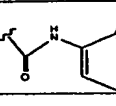

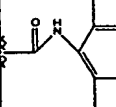
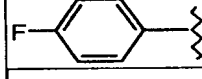
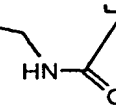
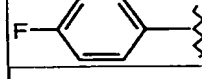
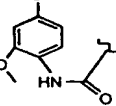
R<sup>2</sup>R<sup>L</sup>

B-1677					
B-1678					
B-1679					
B-1680					
B-1681					
B-1682					
B-1683					
B-1684					
B-1685					
B-1686					

SUBSTITUTE SHEET (RULE 26)

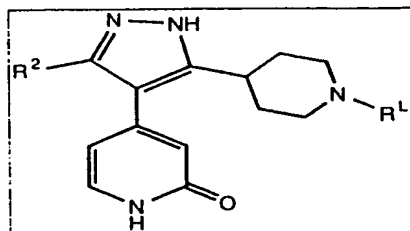
Example#

 $R^2$  $R^L$ 

B-1687					
B-1688					
B-1689					
B-1690					
B-1691					
B-1692					
B-1693					

SUBSTITUTE SHEET (RULE 26)

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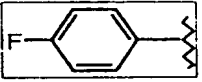
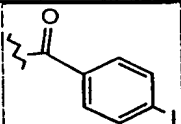
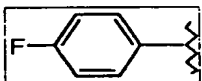
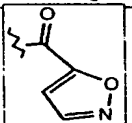
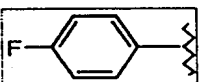
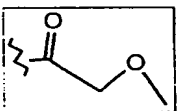
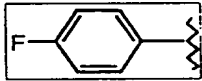
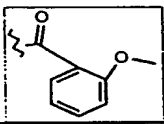
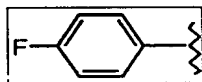
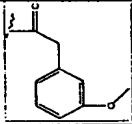
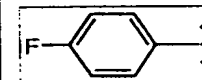
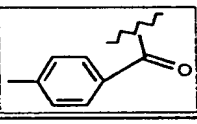
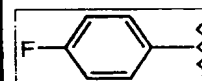
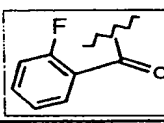
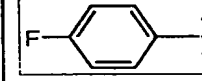
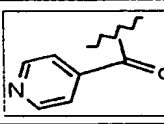
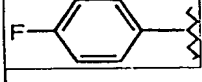
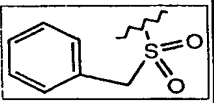

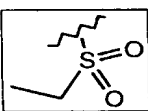
Examples B-1694 through B-1717 are prepared from Scaffold C-66

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1694					
B-1695					
B-1696					
B-1697					
B-1698					
B-1699					
B-1700					

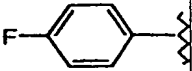
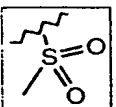
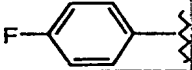
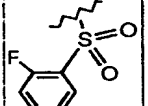

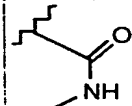

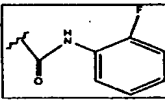
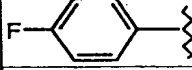
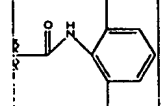
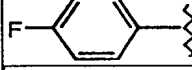
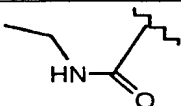
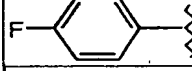
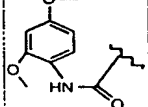
SUBSTITUTE SHEET (RULE 26)

Example#

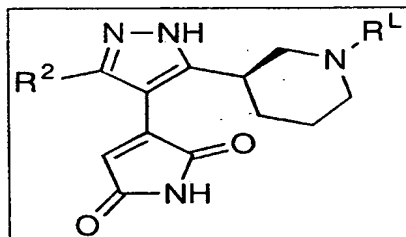
 $R^2$  $R^L$ 

B-1701					
B-1702					
B-1703					
B-1704					
B-1705					
B-1706					
B-1707					
B-1708					
B-1709					
B-1710					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1711					
B-1712					
B-1713					
B-1714					
B-1715					
B-1716					
B-1717					

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Examples B-1718 through B-1741 are prepared from Scaffold C-69

Example#

 $R^2$  $R^L$ 

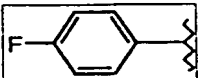
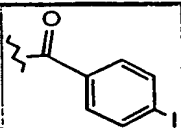
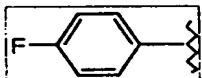
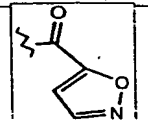
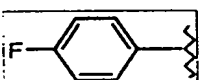
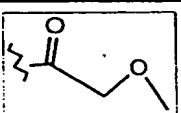
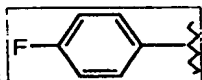
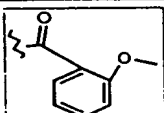
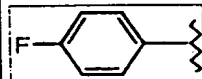
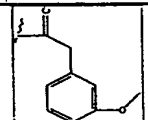
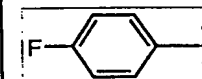
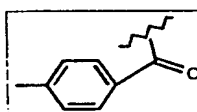
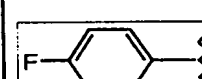
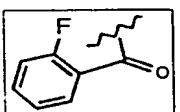
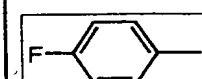
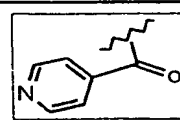
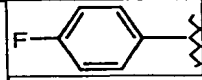
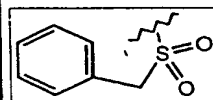
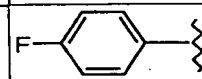
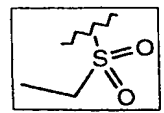
B-1718					
B-1719					
B-1720					
B-1721					
B-1722					
B-1723					
B-1724					

SUBSTITUTESHEET (RULE 26)

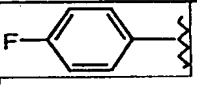
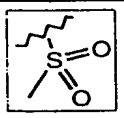
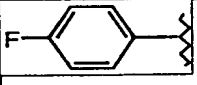
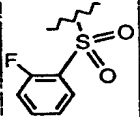
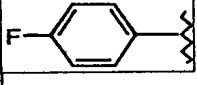
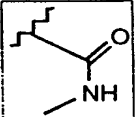
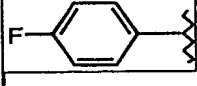
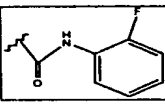

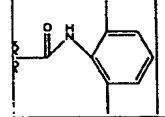

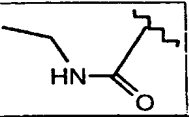
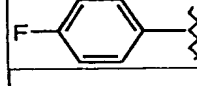
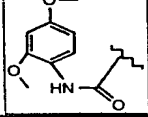


Example#

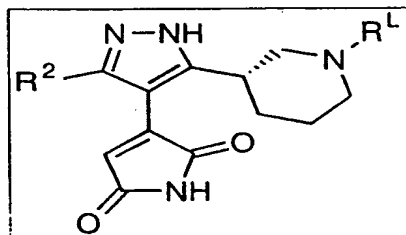
R<sup>2</sup>R<sup>L</sup>

B-1725					
B-1726					
B-1727					
B-1728					
B-1729					
B-1730					
B-1731					
B-1732					
B-1733					
B-1734					

SUBSTITUTESHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1735					
B-1736					
B-1737					
B-1738					
B-1739					
B-1740					
B-1741					

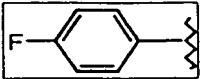
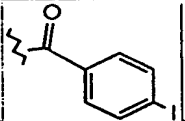
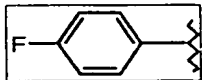
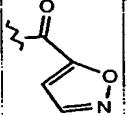
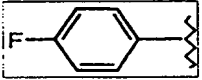
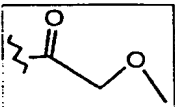
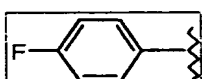
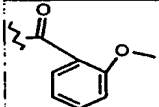
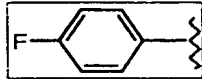
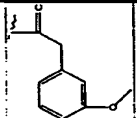
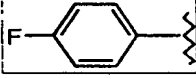
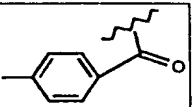
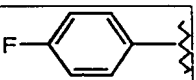
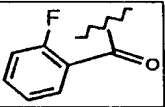
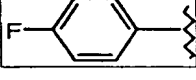
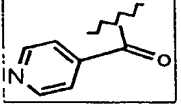
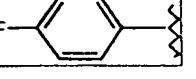
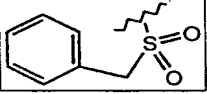
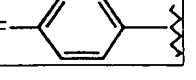
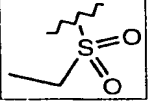
547




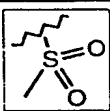

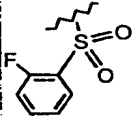
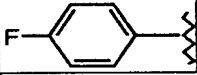
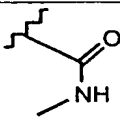

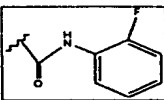

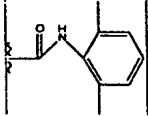

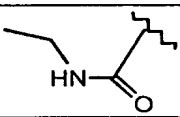
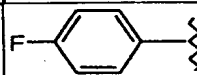
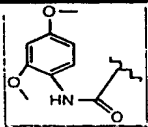
Examples B-1742 through B-1765 are prepared from Scaffold C-70

Example#	$R^2$	$R^1$			
B-1742					
B-1743					
B-1744					
B-1745					
B-1746					
B-1747					
B-1748					

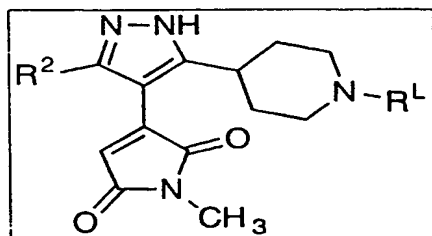
SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1749					
B-1750					
B-1751					
B-1752					
B-1753					
B-1754					
B-1755					
B-1756					
B-1757					
B-1758					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1759					
B-1760					
B-1761					
B-1762					
B-1763					
B-1764					
B-1765					

550



Examples B-1766 through B-1789 are prepared from Scaffold C-71

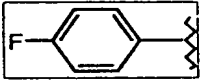
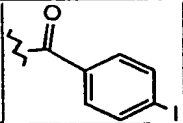
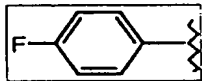
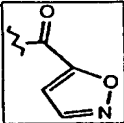
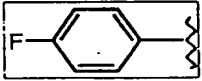
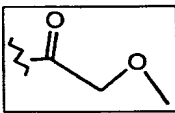
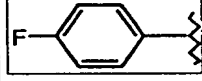
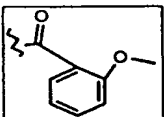
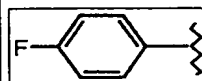
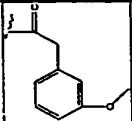
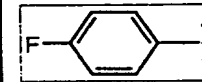
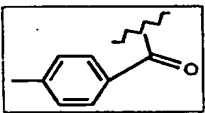
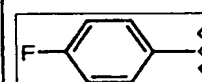
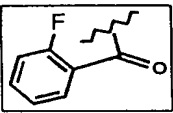
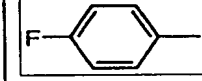
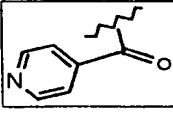
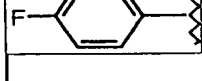
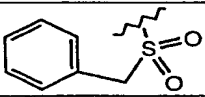
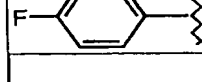
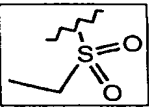
Example#

R²

R¹

B-1766					
B-1767					
B-1768					
B-1769					
B-1770					
B-1771					
B-1772					

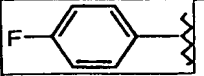
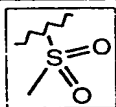
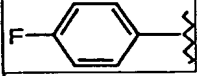
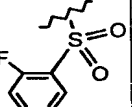

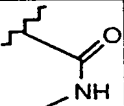
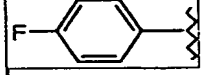
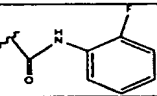
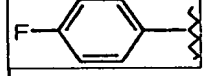
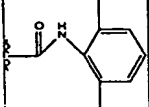
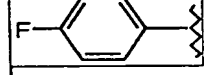
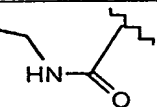
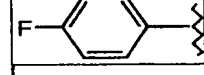
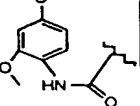
SUBSTITUTESHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1773					
B-1774					
B-1775					
B-1776					
B-1777					
B-1778					
B-1779					
B-1780					
B-1781					
B-1782					

SUBSTITUTESHEET (RULE 26)

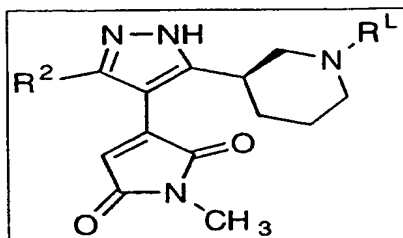
Example#

 $R^2$  $R^L$ 

B-1783					
B-1784					
B-1785					
B-1786					
B-1787					
B-1788					
B-1789					



553



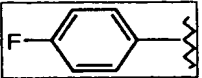
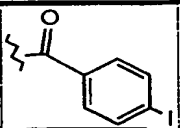
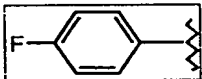
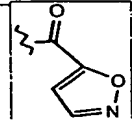
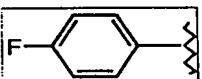
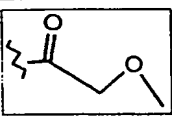

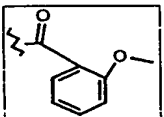
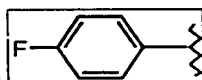
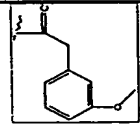
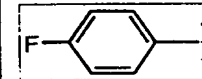
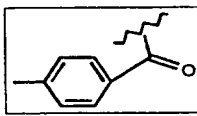
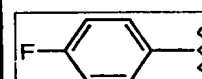
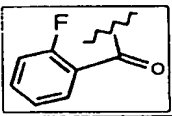
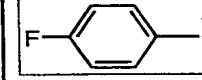
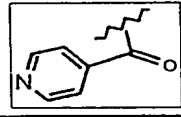
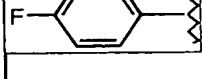
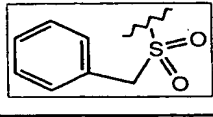
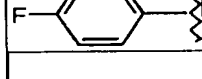
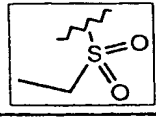
Examples B-1790 through B-1813 are prepared from Scaffold C-72

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1790					
B-1791					
B-1792					
B-1793					
B-1794					
B-1795					
B-1796					

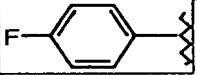
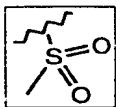
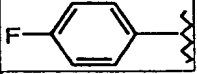
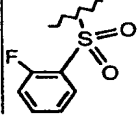
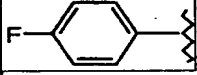
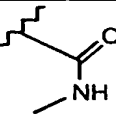
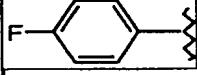
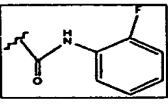

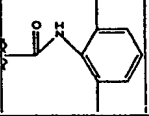
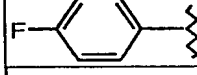
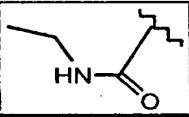
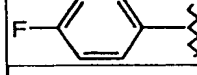
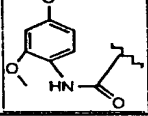
SUBSTITUTE SHEET (RULE 26)

Example#

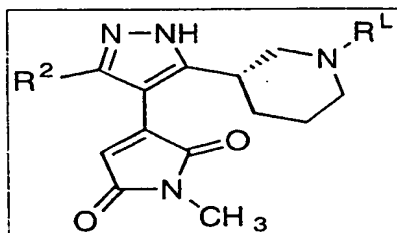
 $R^2$  $R^L$ 

B-1797					
B-1798					
B-1799					
B-1800					
B-1801					
B-1802					
B-1803					
B-1804					
B-1805					
B-1806					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1807					
B-1808					
B-1809					
B-1810					
B-1811					
B-1812					
B-1813					

556



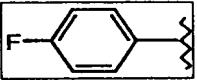
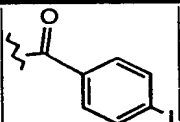
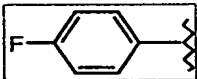
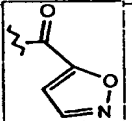
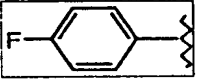
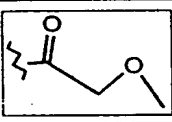
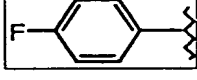
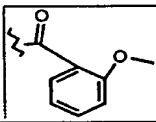
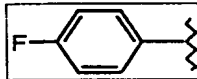
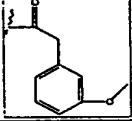
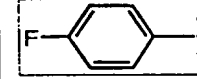
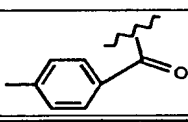
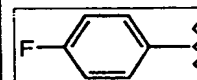
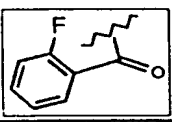
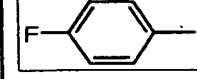
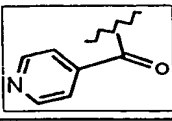
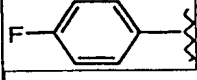
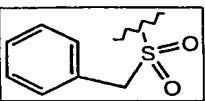

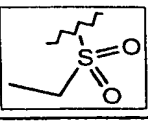
Examples B-1814 through B-1837 are prepared from Scaffold C-73

Example#

 $R^2$  $R^L$ 

B-1814					
B-1815					
B-1816					
B-1817					
B-1818					
B-1819					
B-1820					

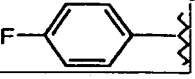
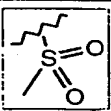
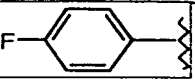
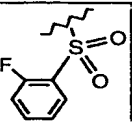
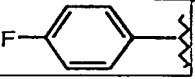
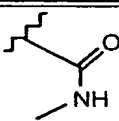
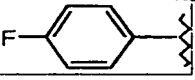
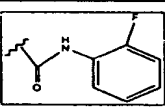
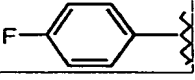
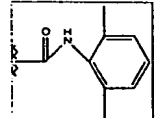
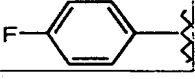
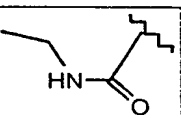
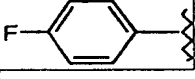
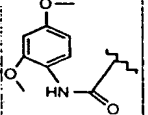
SUBSTITUTESHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1821					
B-1822					
B-1823					
B-1824					
B-1825					
B-1826					
B-1827					
B-1828					
B-1829					
B-1830					

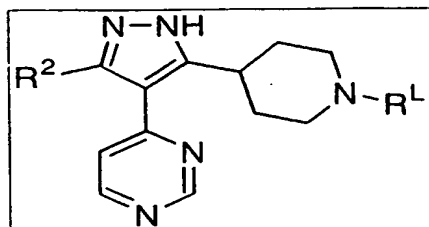
SUBSTITUTESHEET (RULE 26)

Example#

 $R^2$  $R^L$ 

B-1831					
B-1832					
B-1833					
B-1834					
B-1835					
B-1836					
B-1837					

559



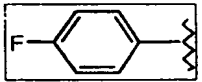
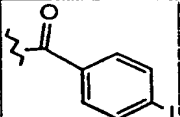
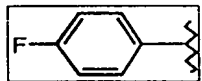
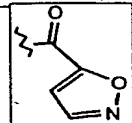
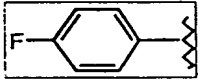
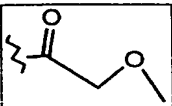

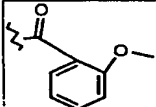
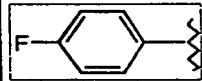
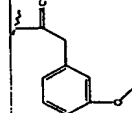
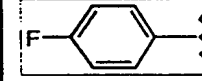
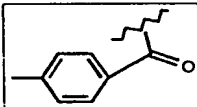
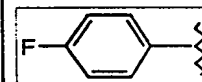
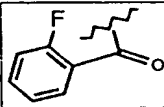
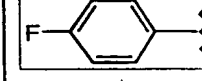
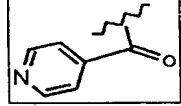
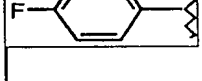

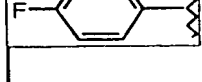
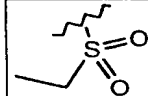
Examples B-1838 through B-1861 are prepared from Scaffold C-33

Example#

R<sup>2</sup>R<sup>1</sup>

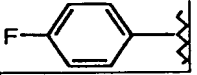
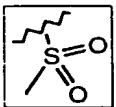
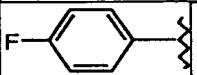
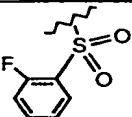

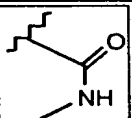

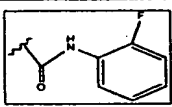

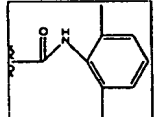

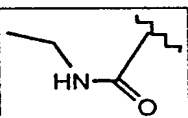
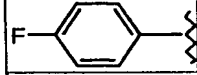
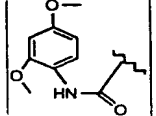
B-1838					
B-1839					
B-1840					
B-1841					
B-1842					
B-1843					
B-1844					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1845					
B-1846					
B-1847					
B-1848					
B-1849					
B-1850					
B-1851					
B-1852					
B-1853					
B-1854					

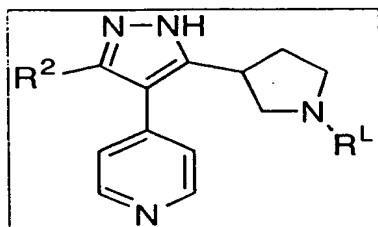
SUBSTITUTE SHEET (RULE 26)



Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1855					
B-1856					
B-1857					
B-1858					
B-1859					
B-1860					
B-1861					

SUBSTITUTE SHEET (RULE 26)

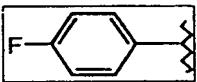
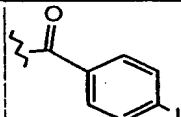
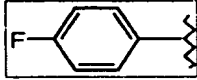
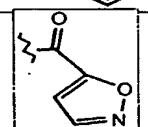
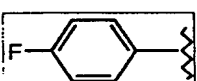
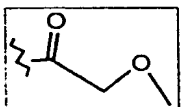
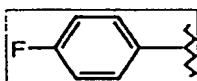
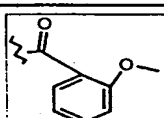
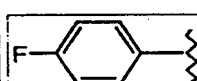
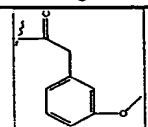
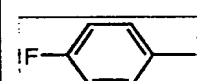
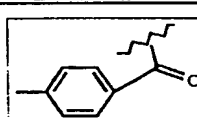
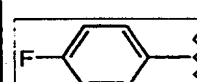
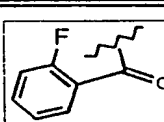
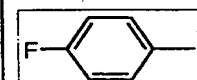
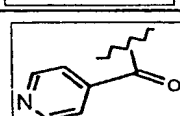
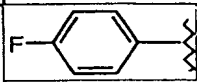
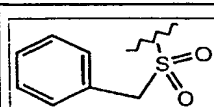
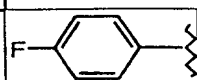
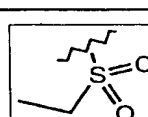
562




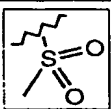

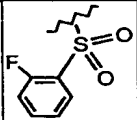
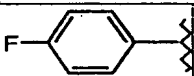
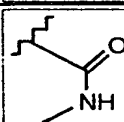
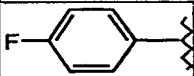
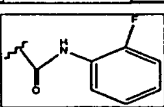

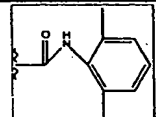

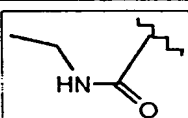
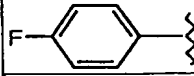
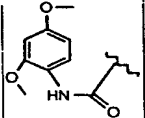
Examples B-1862 through B-1885 are prepared from Scaffold C-45

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1862					
B-1863					
B-1864					
B-1865					
B-1866					
B-1867					
B-1868					

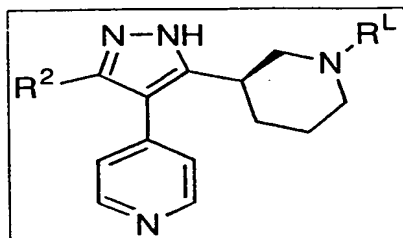
SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1869					
B-1870					
B-1871					
B-1872					
B-1873					
B-1874					
B-1875					
B-1876					
B-1877					
B-1878					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1879					
B-1880					
B-1881					
B-1882					
B-1883					
B-1884					
B-1885					

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Examples B-1886 through B-1909 prepared from Scaffold C-42

Example#


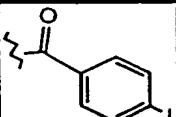
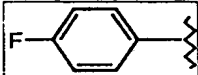
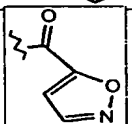
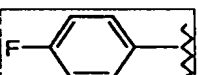
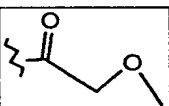

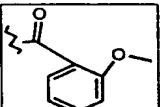
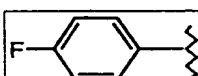
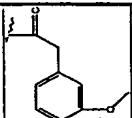
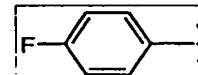
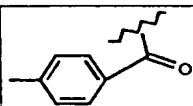
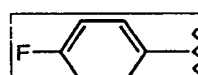
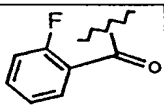
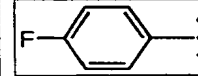
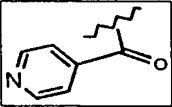
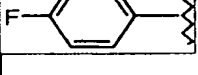
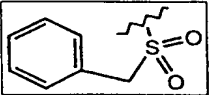
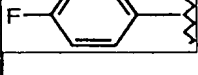
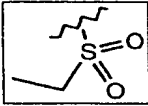
 $R^2$  $R^1$ 

B-1886					
B-1887					
B-1888					
B-1889					
B-1890					
B-1891					
B-1892					

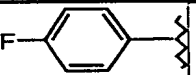
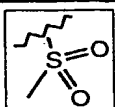
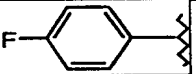
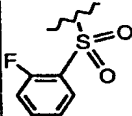

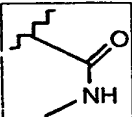

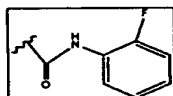
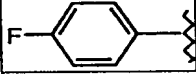
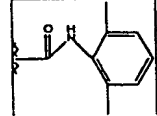
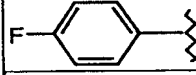
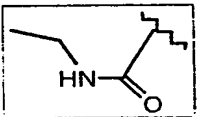
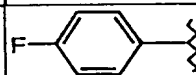
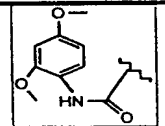
SUBSTITUTESHEET (RULE 26)

Example#

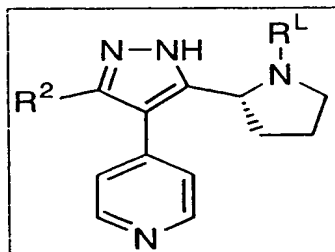
 $R^2$  $R^4$ 

B-1893					
B-1894					
B-1895					
B-1896					
B-1897					
B-1898					
B-1899					
B-1900					
B-1901					
B-1902					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1903					
B-1904					
B-1905					
B-1906					
B-1907					
B-1908					
B-1909					

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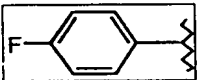
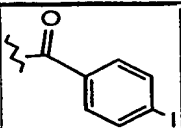
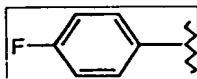
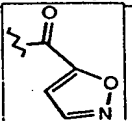
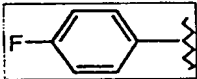
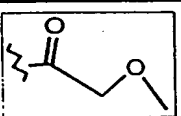
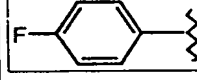
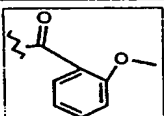
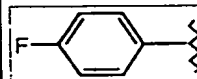
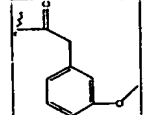
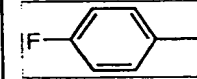
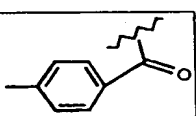
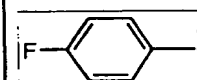
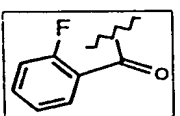
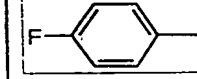
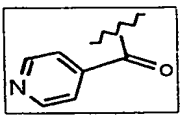

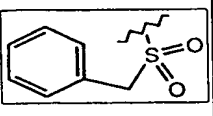
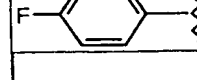
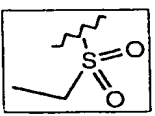


Examples B-1910 through B-1933 are prepared from Scaffold C-44

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-1910					
B-1911					
B-1912					
B-1913					
B-1914					
B-1915					
B-1916					

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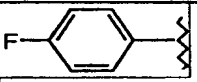
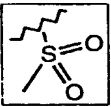
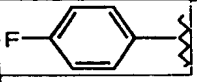
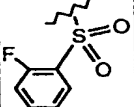
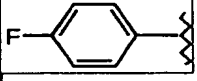
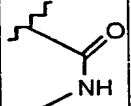
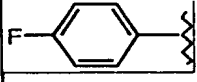
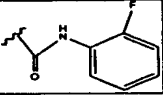

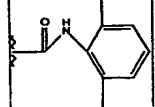

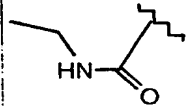
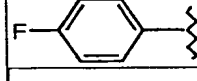
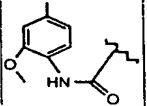


Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1917					
B-1918					
B-1919					
B-1920					
B-1921					
B-1922					
B-1923					
B-1924					
B-1925					
B-1926					

SUBSTITUTE SHEET (RULE 26)

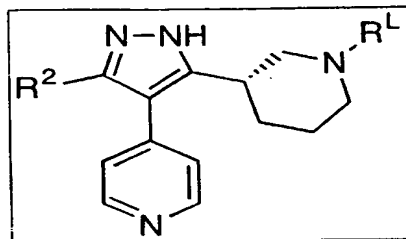
Example#

 $R^2$  $R^1$ 

B-1927					
B-1928					
B-1929					
B-1930					
B-1931					
B-1932					
B-1933					

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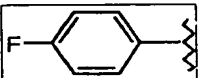
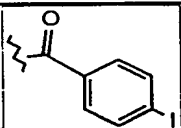
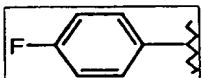
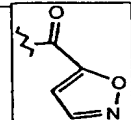
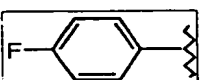
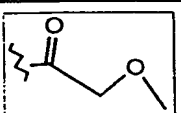
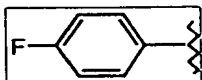
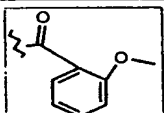

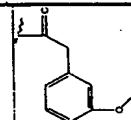
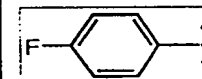
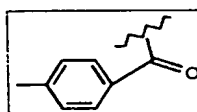
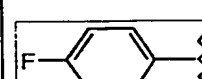
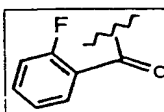
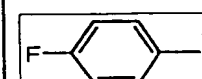
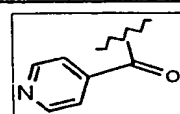

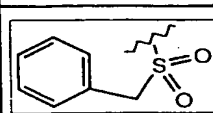
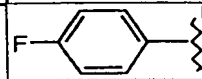
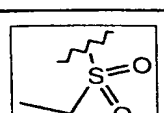
Examples B-1934 through B-1957 are prepared from Scaffold C-41

Example#	R <sup>2</sup>	R <sup>4</sup>			
B-1934					
B-1935					
B-1936					
B-1937					
B-1938					
B-1939					
B-1940					

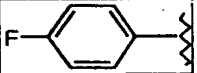
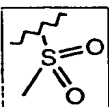
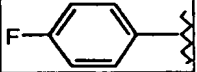
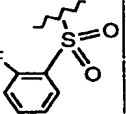

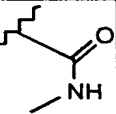

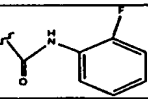

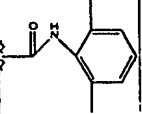
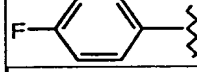
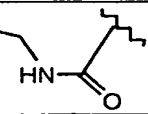
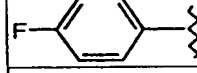
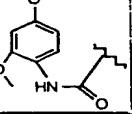
SUBSTITUTE SHEET (RULE 26)

Example#

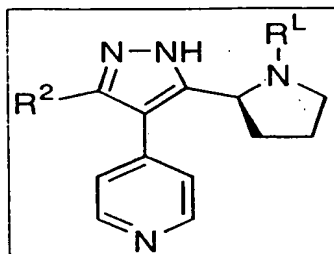
 $R^2$  $R^L$ 

B-1941					
B-1942					
B-1943					
B-1944					
B-1945					
B-1946					
B-1947					
B-1948					
B-1949					
B-1950					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1951					
B-1952					
B-1953					
B-1954					
B-1955					
B-1956					
B-1957					

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Examples B-1958 through B-1981 are prepared from Scaffold C-43


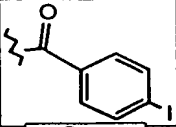
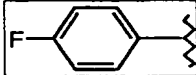
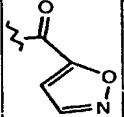

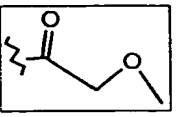
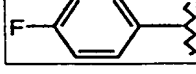
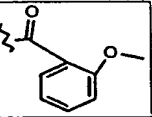
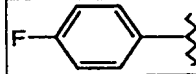
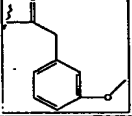
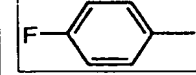
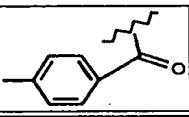
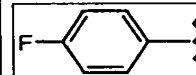
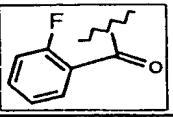
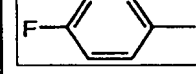
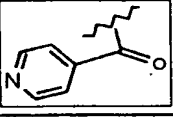
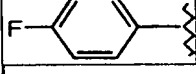
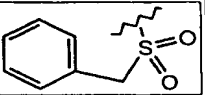

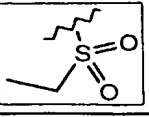
Example#

R²

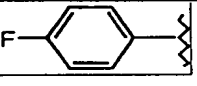
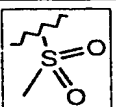
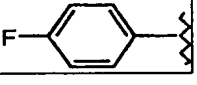
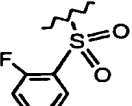
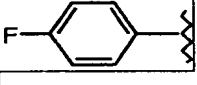
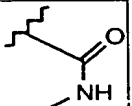
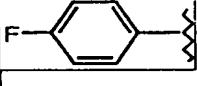
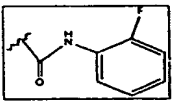
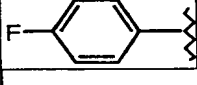
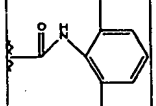
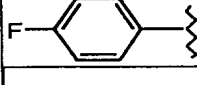
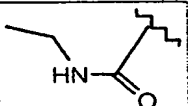
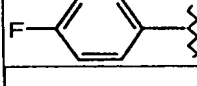
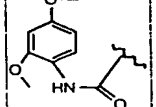
R¹

B-1958					
B-1959					
B-1960					
B-1961					
B-1962					
B-1963					
B-1964					

SUBSTITUTE SHEET (RULE 26)

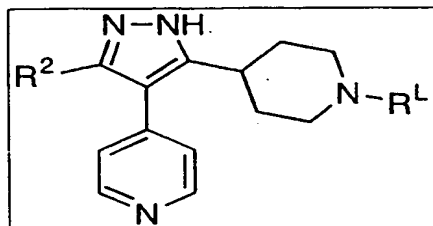
Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1965					
B-1966					
B-1967					
B-1968					
B-1969					
B-1970					
B-1971					
B-1972					
B-1973					
B-1974					

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Example#	R <sup>2</sup>	R <sup>L</sup>			
B-1975					
B-1976					
B-1977					
B-1978					
B-1979					
B-1980					
B-1981					



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Examples B-1982 through B-2005 are prepared from Scaffold C-30

Example#

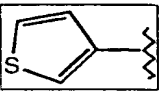
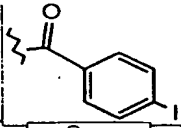
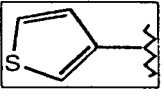
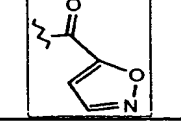
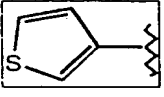
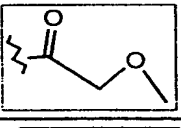
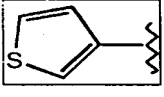
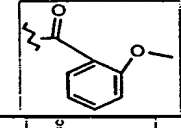
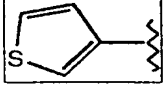
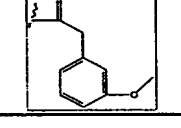
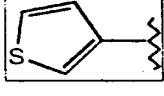
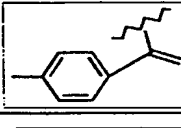
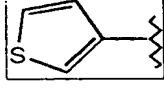
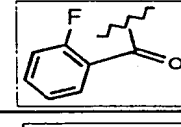
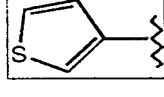
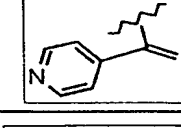
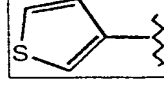
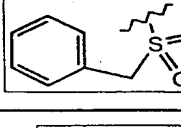
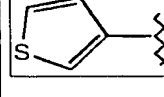
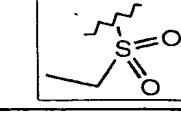
R<sup>2</sup>R<sup>L</sup>

B-1982					
B-1983					
B-1984					
B-1985					
B-1986					
B-1987					
B-1988					

SUBSTITUTE SHEET (RULE 26)

Example#

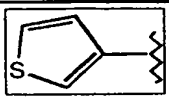
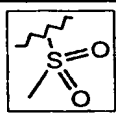
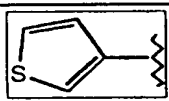
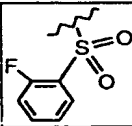
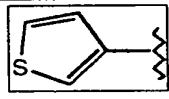
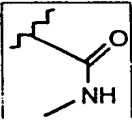
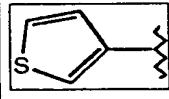
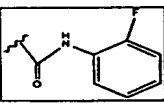
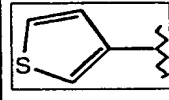
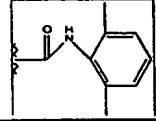
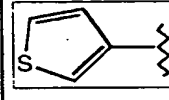
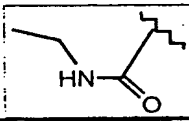
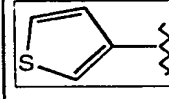
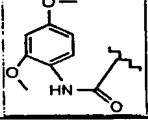
 $R^2$  $R^L$ 

B-1989					
B-1990					
B-1991					
B-1992					
B-1993					
B-1994					
B-1995					
B-1996					
B-1997					
B-1998					

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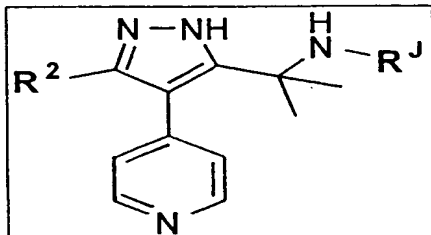
Example#

 $R^2$  $R^L$ 

B-1999					
B-2000					
B-2001					
B-2002					
B-2003					
B-2004					
B-2005					

SUBSTITUTE SHEET (RULE 26)

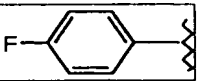
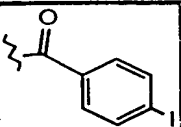
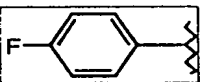
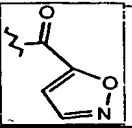
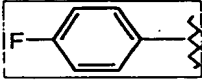
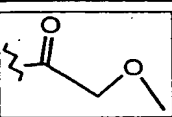
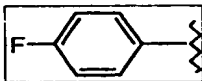
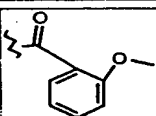
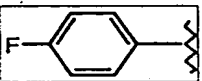
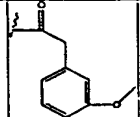
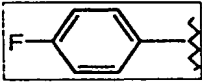
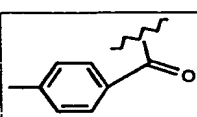

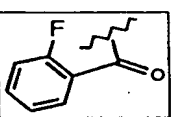
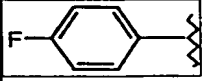
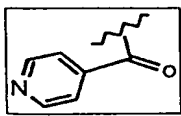
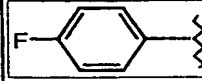
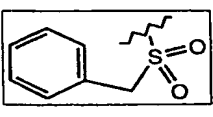
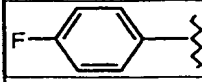
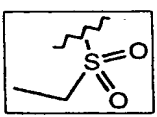
580

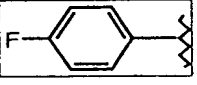
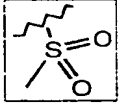
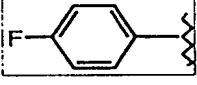
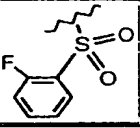
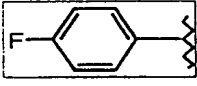
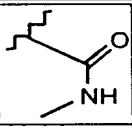
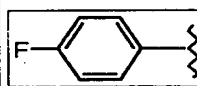
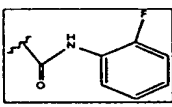
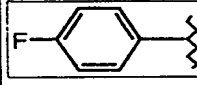
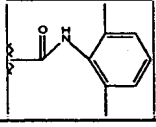
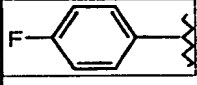
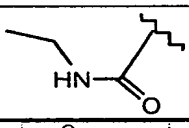
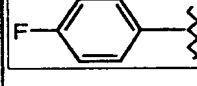
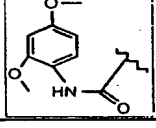


Examples B-2006 through B-2029 are prepared from Scaffold C-60

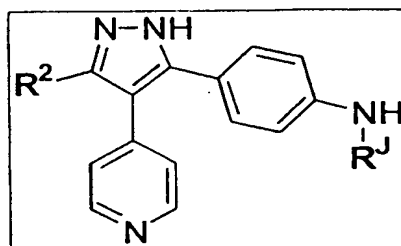
Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2006					
B-2007					
B-2008					
B-2009					
B-2010					
B-2011					
B-2012					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2013					
B-2014					
B-2015					
B-2016					
B-2017					
B-2018					
B-2019					
B-2020					
B-2021					
B-2022					

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2023					
B-2024					
B-2025					
B-2026					
B-2027					
B-2028					
B-2029					

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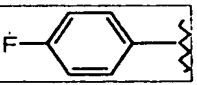
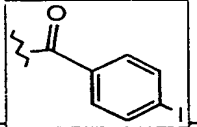
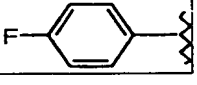
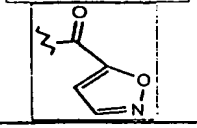
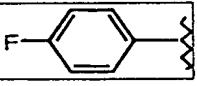
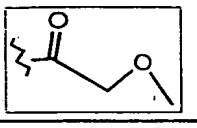
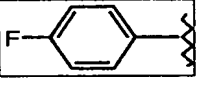
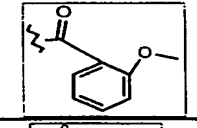
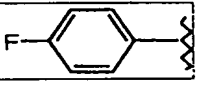
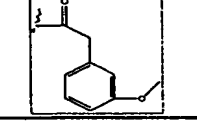
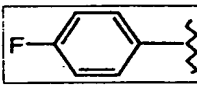
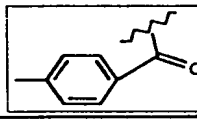
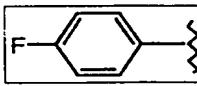
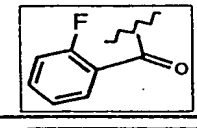

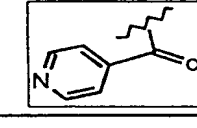
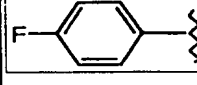
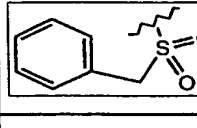
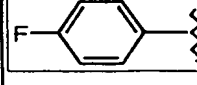
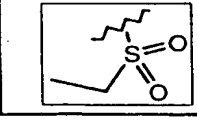
Examples B-2030 through B-2053 are prepared from Scaffold C-36

Example#

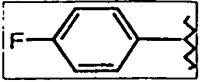
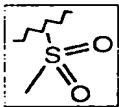
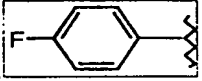
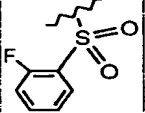
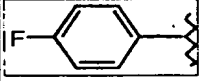
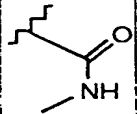
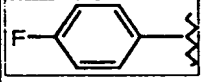
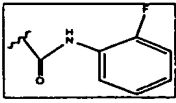
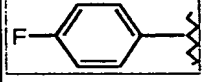
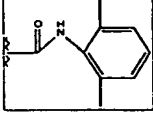
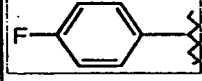
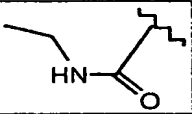

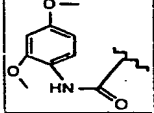
R<sup>2</sup>R<sup>1</sup>

B-2030					
B-2031					
B-2032					
B-2033					
B-2034					
B-2035					
B-2036					

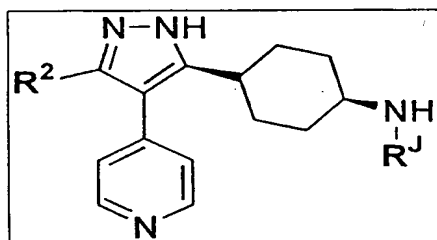
SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2037					
B-2038					
B-2039					
B-2040					
B-2041					
B-2042					
B-2043					
B-2044					
B-2045					
B-2046					



Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2047					
B-2048					
B-2049					
B-2050					
B-2051					
B-2052					
B-2053					

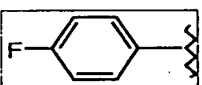
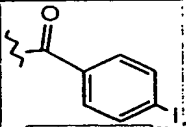
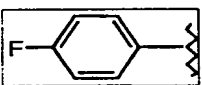
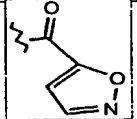
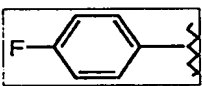
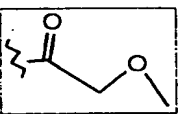
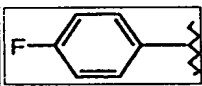
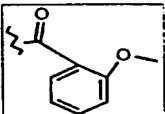
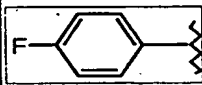
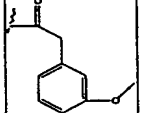

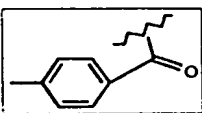

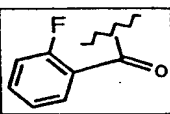
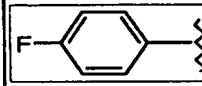
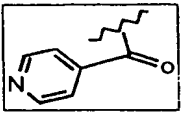
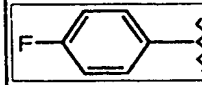
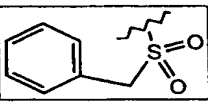
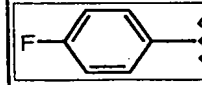
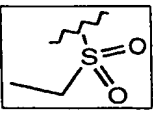
586


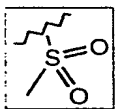
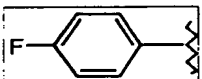
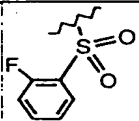
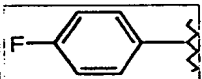
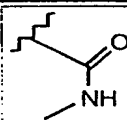
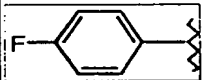
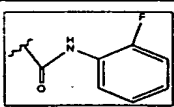
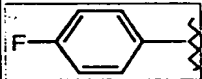
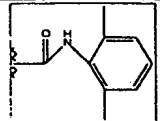

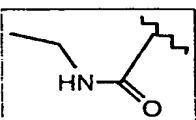

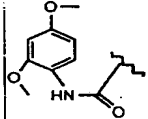


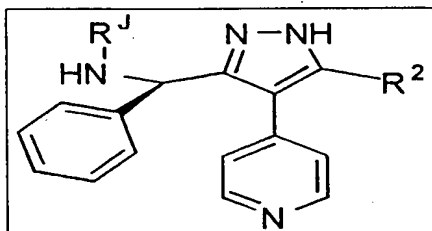
Examples B-2054 through B-2077 are prepared from Scaffold C-34

Example#	R <sup>2</sup>	R <sup>ʲ</sup>			
B-2054					
B-2055					
B-2056					
B-2057					
B-2058					
B-2059					
B-2060					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2061					
B-2062					
B-2063					
B-2064					
B-2065					
B-2066					
B-2067					
B-2068					
B-2069					
B-2070					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2071					
B-2072					
B-2073					
B-2074					
B-2075					
B-2076					
B-2077					



Examples B-2078 through B-2101 are prepared from Scaffold C-57

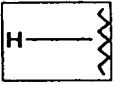
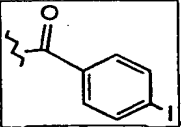
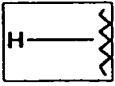
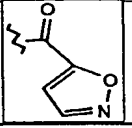
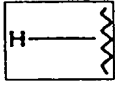
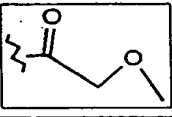
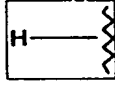
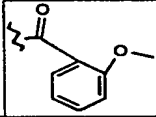
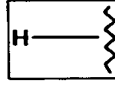
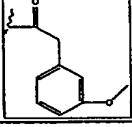
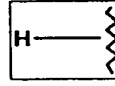
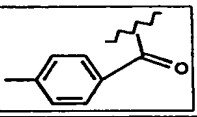
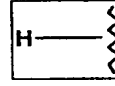
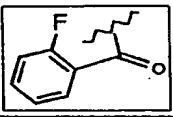
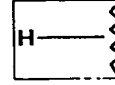
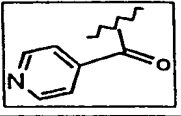
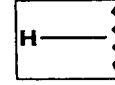
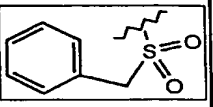
Example#

$R^2$

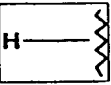
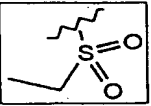
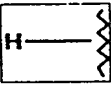
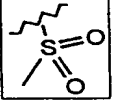
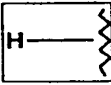
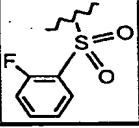
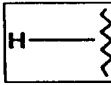
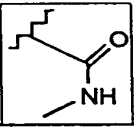

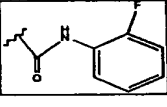
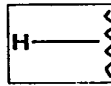
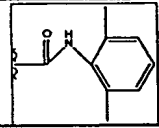
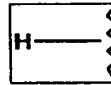
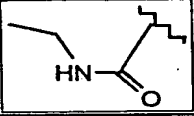
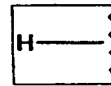
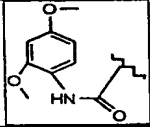
$R^J$

B-2078					
B-2079					
B-2080					
B-2081					
B-2082					
B-2083					
B-2084					

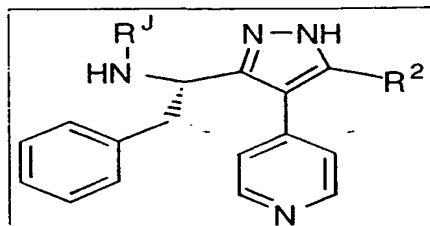
SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2085					
B-2086					
B-2087					
B-2088					
B-2089					
B-2090					
B-2091					
B-2092					
B-2093					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2094					
B-2095					
B-2096					
B-2097					
B-2098					
B-2099					
B-2100					
B-2101					

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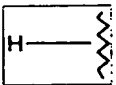
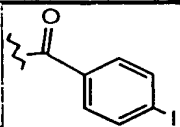
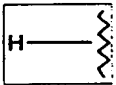
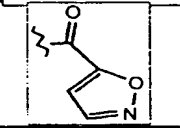
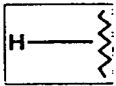
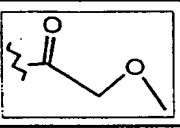
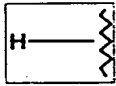
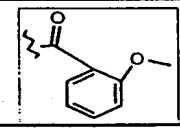
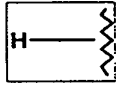
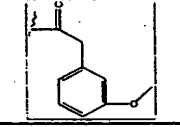
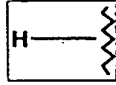
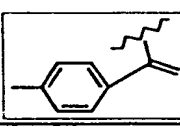
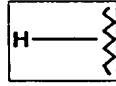
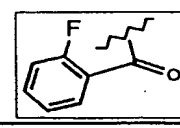
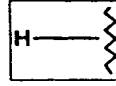
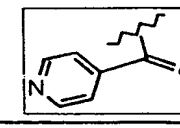
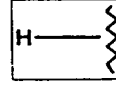
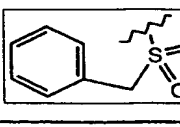
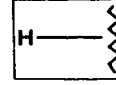
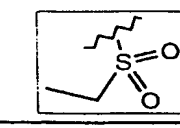


Examples B-2102 through B-2125 are prepared from Scaffold C-52

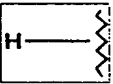
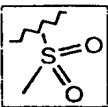
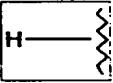
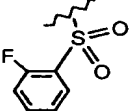
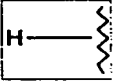
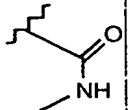
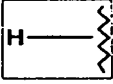
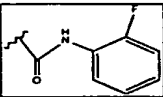
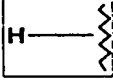
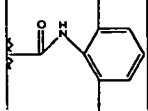
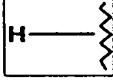
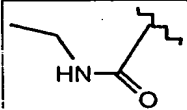
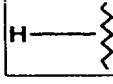
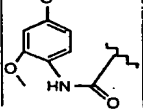
Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2102					
B-2103					
B-2104					
B-2105					
B-2106					
B-2107					
B-2108					

SUBSTITUTE SHEET (RULE 26)

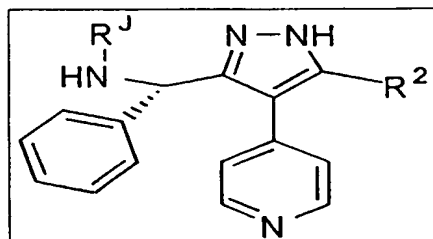


Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2109					
B-2110					
B-2111					
B-2112					
B-2113					
B-2114					
B-2115					
B-2116					
B-2117					
B-2118					

SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2119					
B-2120					
B-2121					
B-2122					
B-2123					
B-2124					
B-2125					

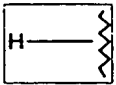
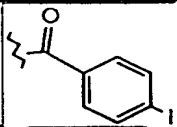
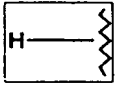
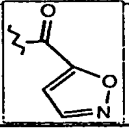
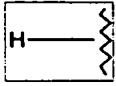
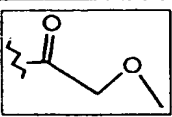
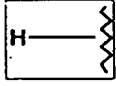
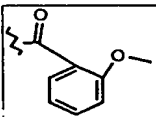
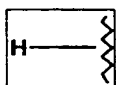
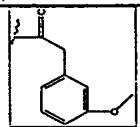
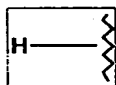
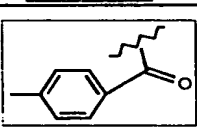
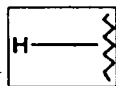
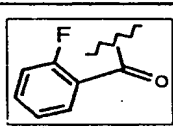
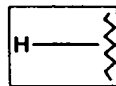
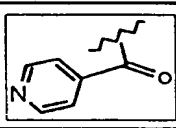
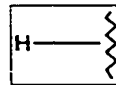
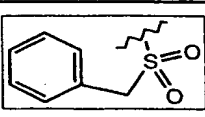
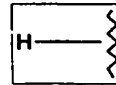
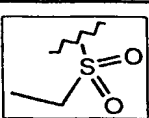
595



Examples B-2126 through B-2149 are prepared from Scaffold C-56

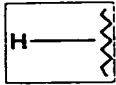
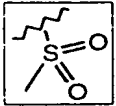
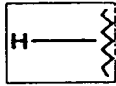
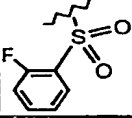
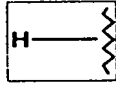
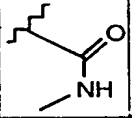
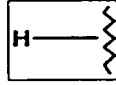
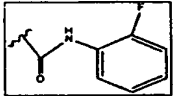
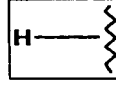
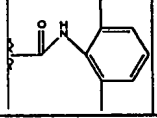
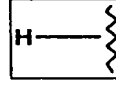
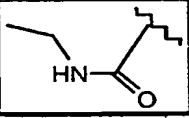
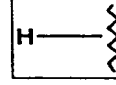
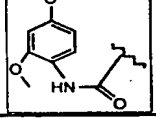
Example#	$R^2$	$R^J$			
B-2126					
B-2127					
B-2128					
B-2129					
B-2130					
B-2131					
B-2132					

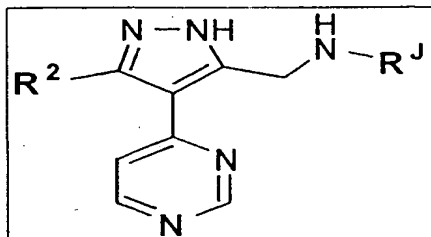
SUBSTITUTE SHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2133					
B-2134					
B-2135					
B-2136					
B-2137					
B-2138					
B-2139					
B-2140					
B-2141					
B-2142					

Example#

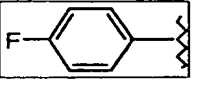
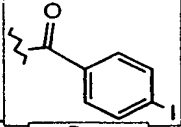
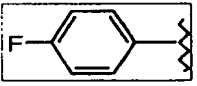
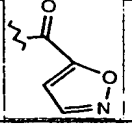
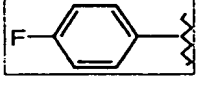
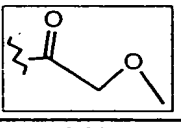
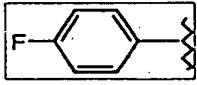
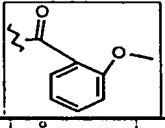
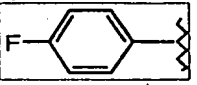
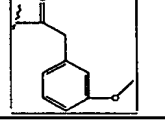
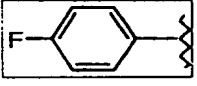
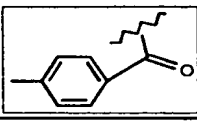
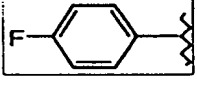
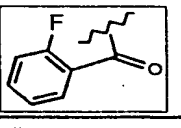
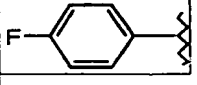
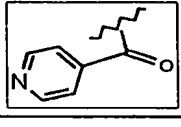
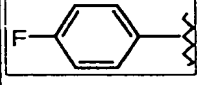
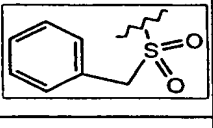
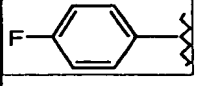
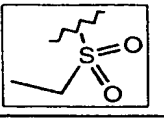
 $R^2$  $R^1$ 

B-2143					
B-2144					
B-2145					
B-2146					
B-2147					
B-2148					
B-2149					

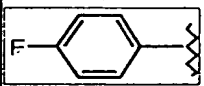
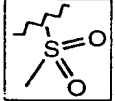
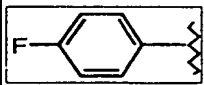
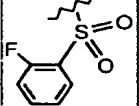
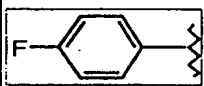
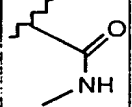
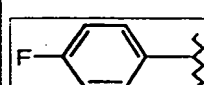
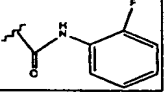
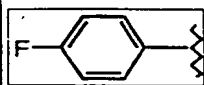
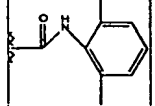
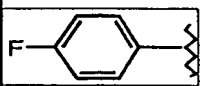
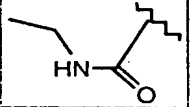
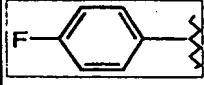
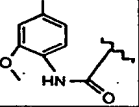


Examples B-2150 through B-2173 are prepared from Scaffold C-32

Example#	$R^2$	$R^J$			
B-2150					
B-2151					
B-2152					
B-2153					
B-2154					
B-2155					
B-2156					

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2157					
B-2158					
B-2159					
B-2160					
B-2161					
B-2162					
B-2163					
B-2164					
B-2165					
B-2166					

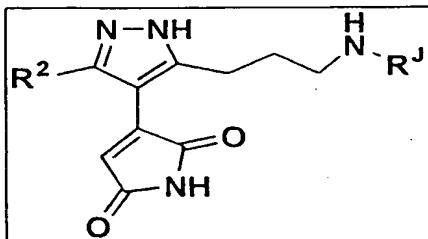
600

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2167					
B-2168					
B-2169					
B-2170					
B-2171					
B-2172					
B-2173					

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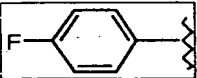
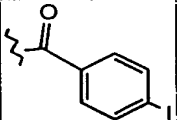
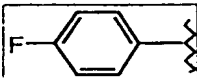
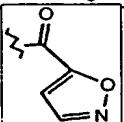
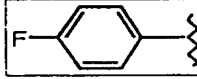
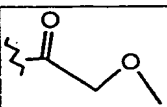
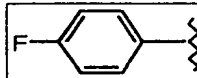
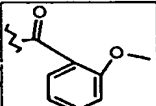
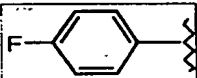
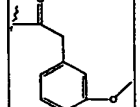

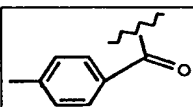

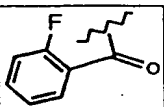

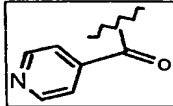
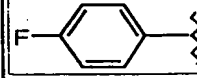
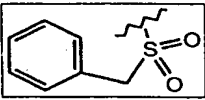
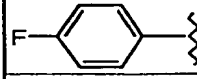
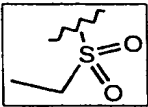
601

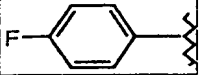
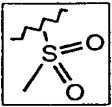
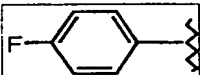
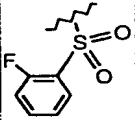
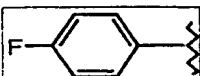
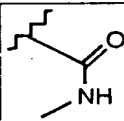
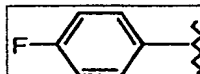
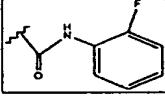
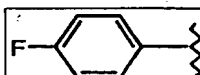
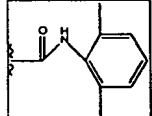
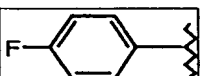
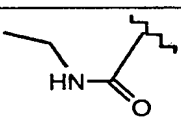
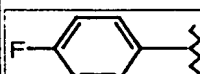
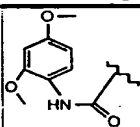


Examples 2174 through B-2197 are prepared from Scaffold C-64

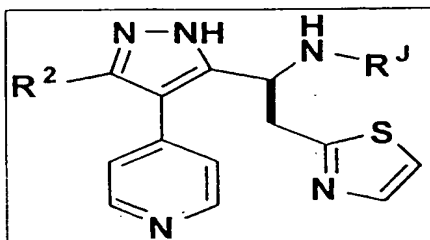
Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2174					
B-2175					
B-2176					
B-2177					
B-2178					
B-2179					
B-2180					

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Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2181					
B-2182					
B-2183					
B-2184					
B-2185					
B-2186					
B-2187					
B-2188					
B-2189					
B-2190					

Example#	R <sup>2</sup>	R <sup>4</sup>			
B-2191					
B-2192					
B-2193					
B-2194					
B-2195					
B-2196					
B-2197					

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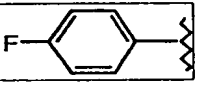
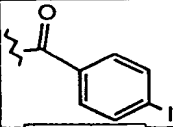
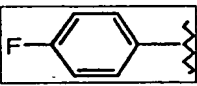
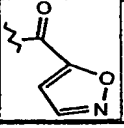
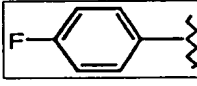
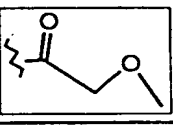
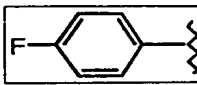
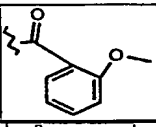
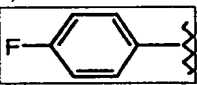
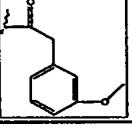

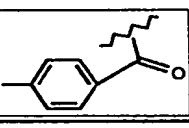
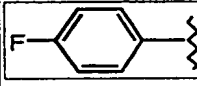
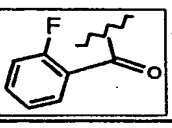
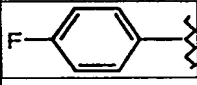
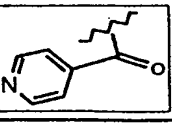
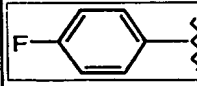
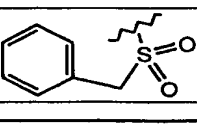

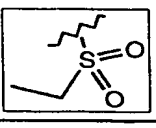


Examples B-2198 through B-2221 re prepared from Scaffold C-22

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2198					
B-2199					
B-2200					
B-2201					
B-2202					
B-2203					
B-2204					

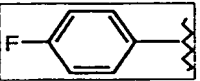
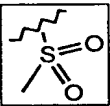
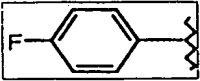
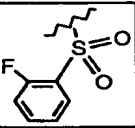
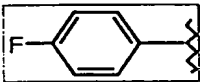
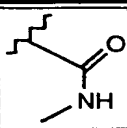
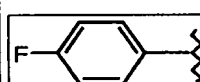
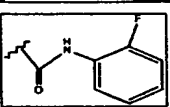

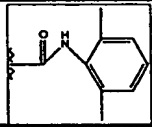

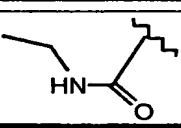
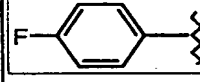
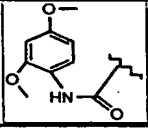
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Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2205					
B-2206					
B-2207					
B-2208					
B-2209					
B-2210					
B-2211					
B-2212					
B-2213					
B-2214					

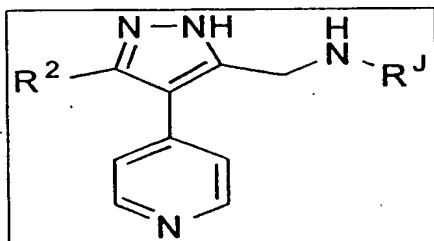
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Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2215					
B-2216					
B-2217					
B-2218					
B-2219					
B-2220					
B-2221					

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607



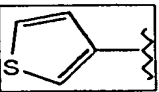
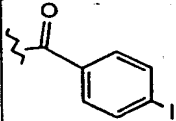
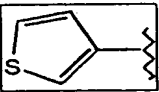
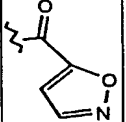
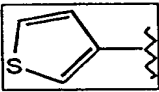
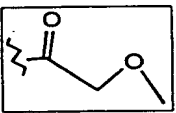
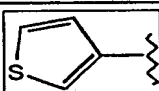
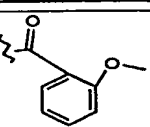
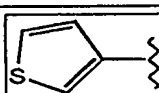
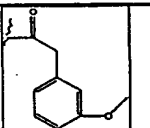
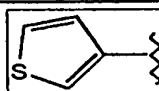
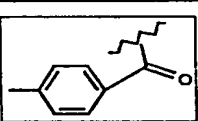
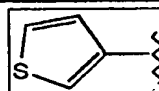
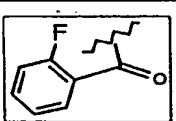
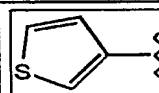
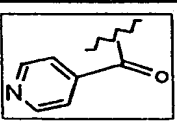
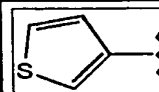
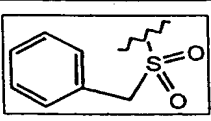
Examples B-2222 through B-2245 are prepared from Scaffold C-29

Example#

 $R^2$  $R^J$ 

B-2222					
B-2223					
B-2224					
B-2225					
B-2226					
B-2227					
B-2228					

SUBSTITUTE SHEET (RULE 26)

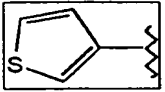
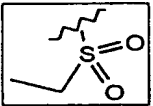
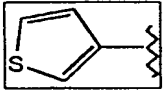
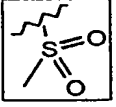
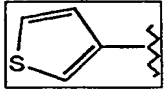
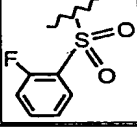
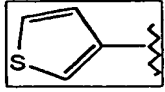
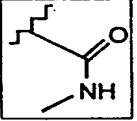
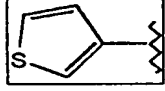
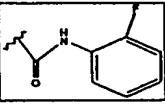
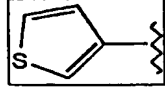
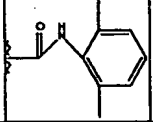
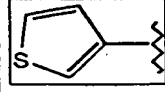
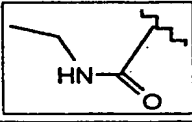
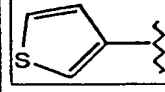
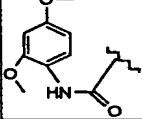
Example#	R <sup>2</sup>	R <sup>3</sup>			
B-2229					
B-2230					
B-2231					
B-2232					
B-2233					
B-2234					
B-2235					
B-2236					
B-2237					

SUBSTITUTE SHEET (RULE 26)



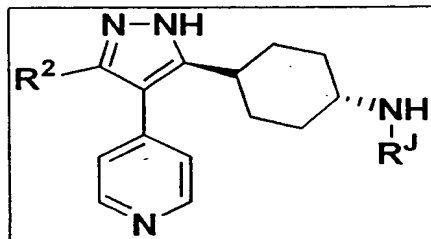
Example#

 $R^2$  $R^J$ 

B-2238					
B-2239					
B-2240					
B-2241					
B-2242					
B-2243					
B-2244					
B-2245					

SUBSTITUTE SHEET (RULE 26)

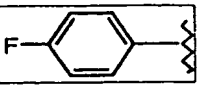
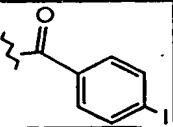
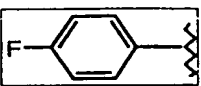
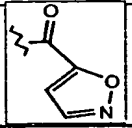
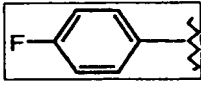
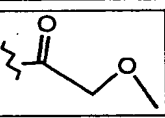
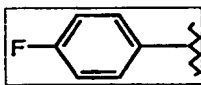
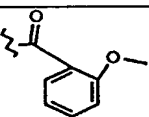
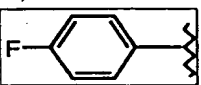
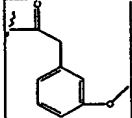
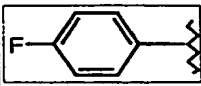
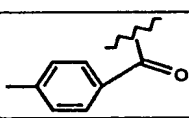
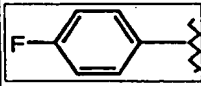
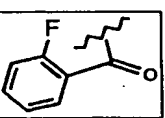
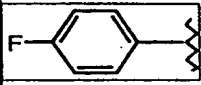
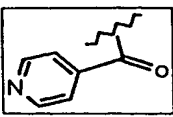

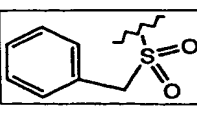
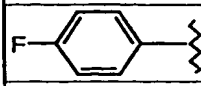
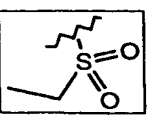
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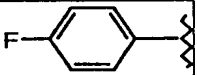
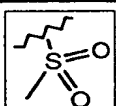
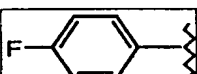
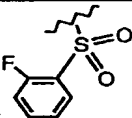
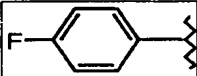
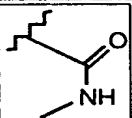

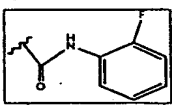

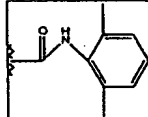

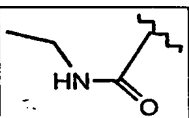
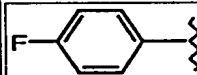
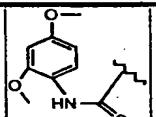


Examples B-2246 through B-2269 are prepared from Scaffold C-35

Example#	R <sup>2</sup>	R <sup>j</sup>			
B-2246					
B-2247					
B-2248					
B-2249					
B-2250					
B-2251					
B-2252					

SUBSTITUTESHEET (RULE 26)

Example#	R <sup>2</sup>	R <sup>1</sup>			
B-2253					
B-2254					
B-2255					
B-2256					
B-2257					
B-2258					
B-2259					
B-2260					
B-2261					
B-2262					

Example#	R <sup>2</sup>	R <sup>J</sup>			
B-2263					
B-2264					
B-2265					
B-2266					
B-2267					
B-2268					
B-2269					

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**Examples B-2270 through B-2317**

15

In a parallel array reaction block containing 48 fritted vessels, each reaction vessel was charged with 250 mg of polymer bound carbodiimide **B48** (1.0 mmol/g resin) and a solution of the acid-containing scaffold **C-49** in dimethylformamide (0.1 M, 500 uL). To each slurry was added a solution of pyridine in dichloromethane (0.2 M, 1000 uL) followed by a solution of a unique amine **B47** (0.2 M, 375 uL) in dimethylformamide. The reaction mixtures were agitated on a Labline benchtop orbital shaker at 250 RPM for 16-20 h at ambient temperature. The reaction mixtures were filtered into conical vials and the polymer was washed with 1.5 mL of dimethylformamide and 2.0 mL of dichloromethane. The filtrates were evaporated to dryness in a Savant apparatus and dimethylformamide (350 uL) was added to each conical vial to dissolve the residue. A solution of tetrafluorophthalic anhydride (1.0 M, 150 uL) in

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dimethylformamide was added to the reconstituted conical vials and the mixture incubated for 2 hours at ambient temperature. Polyamine polymer B33 (4.0 meq N/g resin, 250 mg) and 1.0 mL dichloromethane was then added to the  
5 reaction mixture in each conical vial. After agitating the reaction mixtures for 16 h at 250 RPM on an orbital shaker at ambient temperature, the mixtures were filtered through a polypropylene syringe tube fitted with a porous frit. The polymers were washed twice with  
10 dimethylformamide (1.0 mL each) and the filtrates and washings collected in conical vials. The filtrates were evaporated to dryness and weighed to afford the desired amide products B-2270 through B-2317 as oils or solids. The analytical data and yields for the products prepared  
15 in this manner are listed below.

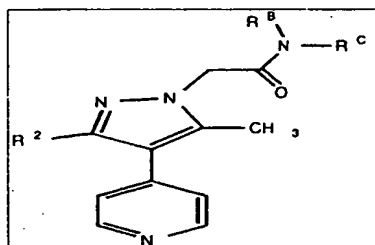
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**SUBSTITUTE SHEET (RULE 26)**

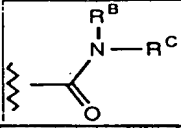
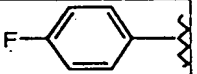
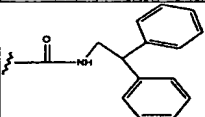
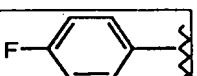
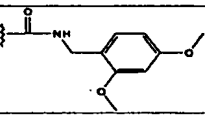
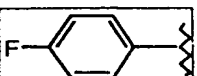
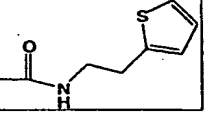
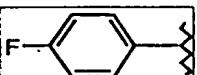
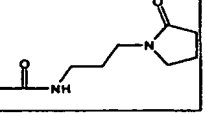
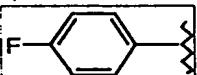
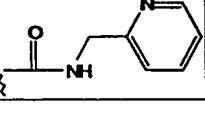
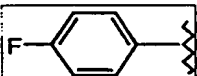
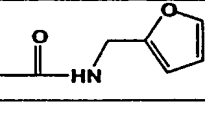
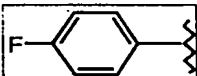
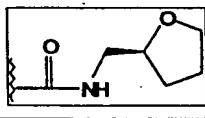
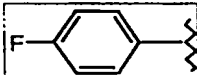
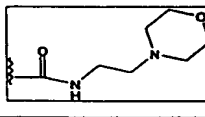

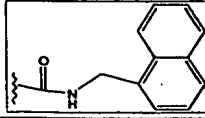
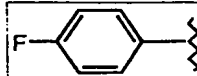
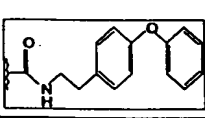
615



	R <sup>2</sup>		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2270			12	352	353
B-2271			39	432	433
B-2272			26	400	-
B-2273			14	396	397
B-2274			30	434	435
B-2275			43	443	-
B-2276			35	364	365

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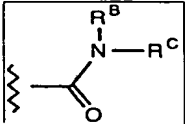

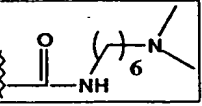


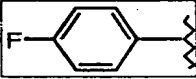
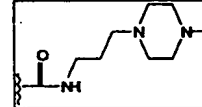

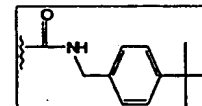

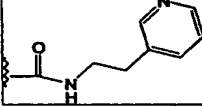
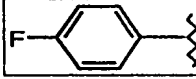
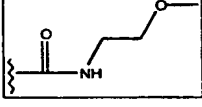
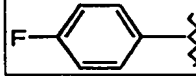
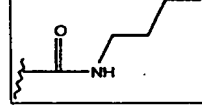
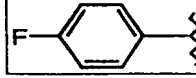
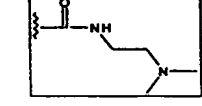
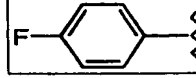
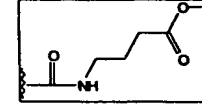
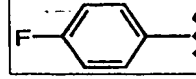
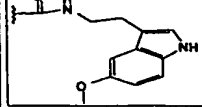
616

	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2277			33	490	-
B-2278			53	460	461
B-2279			10	420	-
B-2280			7	435	436
B-2281			18	401	402
B-2282			22	390	413 <sup>a</sup> <sup>a</sup> M+Na
B-2283			10	394	417 <sup>a</sup> <sup>a</sup> M+Na
B-2284			7	423	-
B-2285			23	450	-
B-2286			4	506	-

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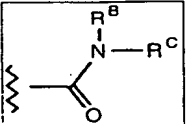
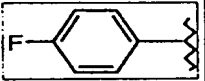
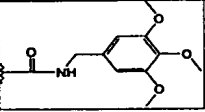
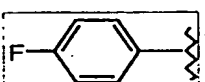
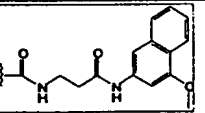
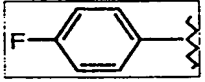
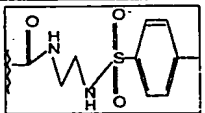
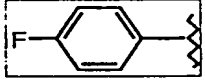
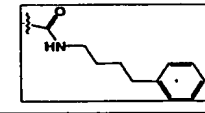
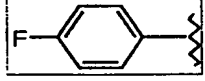
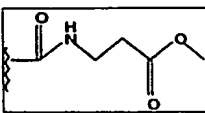
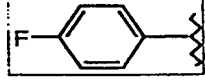
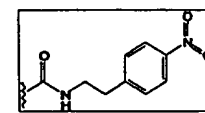
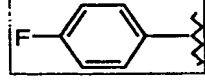
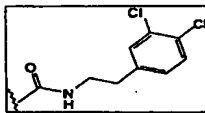
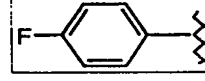
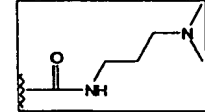
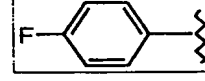
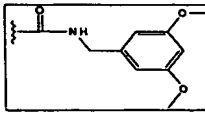
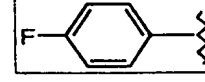
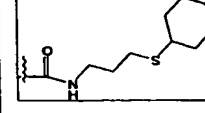


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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2287			5	437	438
B-2288			8	435	436
B-2289			4	450	451
B-2290			9	456	457
B-2291			9	415	416
B-2292			5	368	369
B-2293			5	366	367
B-2294			5	381	382
B-2295			16	410	411
B-2296			4	483	-

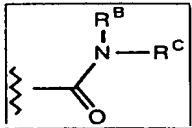
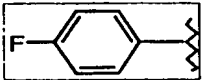
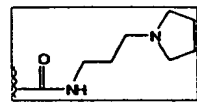
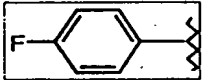
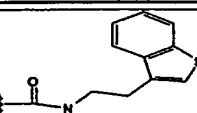
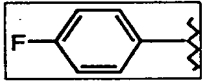
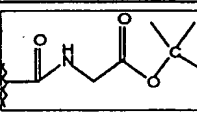

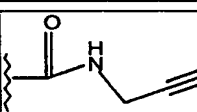
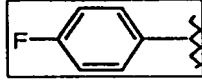
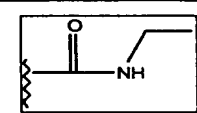

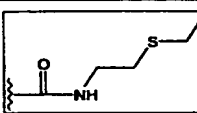
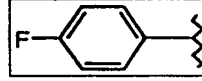
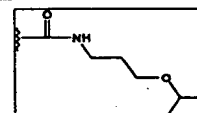
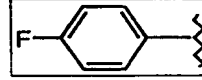
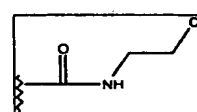
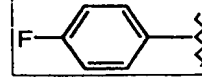
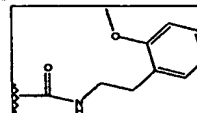
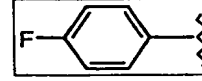
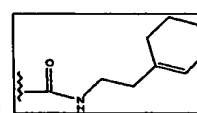
SUBSTITUTE SHEET (RULE 26)

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2297			7	490	-
B-2298			4	537	-
B-2299			4	507	508
B-2300			7	442	-
B-2301			20	396	397
B-2302			30	459	-
B-2303			6	482	-
B-2304			5	395	396
B-2305			10	460	-
B-2306			11	466	467

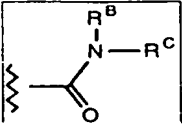
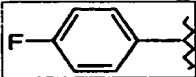
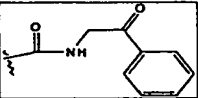
SUBSTITUTE SHEET (RULE 26)

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2307			5	421	422
B-2308			26	470	-
B-2309			24	424	425
B-2310			9	348	-
B-2311			21	338	339
B-2312			28	398	399
B-2313			6	410	-
B-2314			15	363	364
B-2315			11	444	-
B-2316			11	418	-

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620

$R^2$			Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2317			36	428	-

SUBSTITUTE SHEET (RULE 26)

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10

By analogy to the procedure identified above for the preparation of Examples B-2270 through B-2317, the following examples B-2318 through B-2461 were prepared.

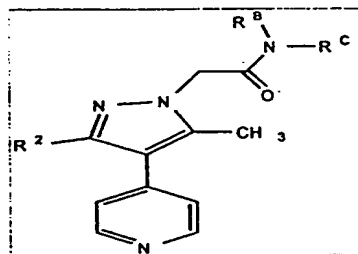
15

20

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30

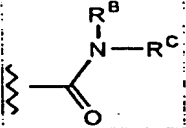
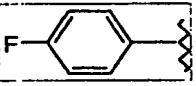
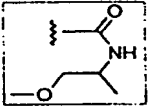
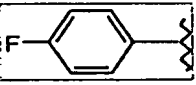
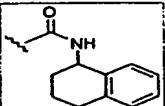
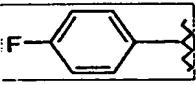
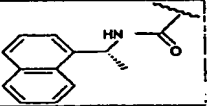
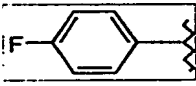
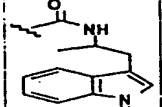
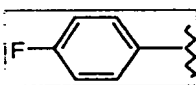
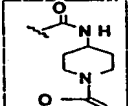
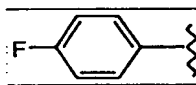
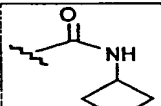
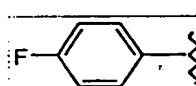
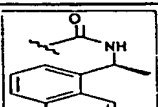
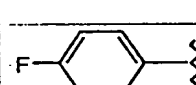
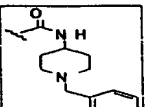
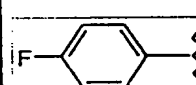
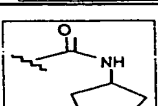
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	R <sup>2</sup>		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2318			23	426	427
B-2319			23	394	-
B-2320			50	490	491
B-2321			49	426	427
B-2322			40	366	367
B-2323			68	410	411
B-2324			57	456	457

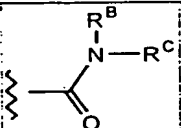
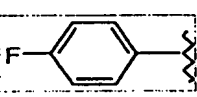
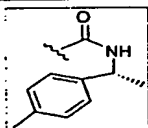
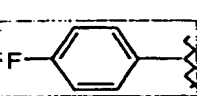
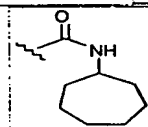
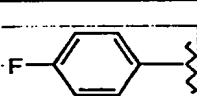
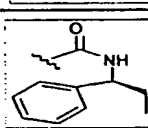
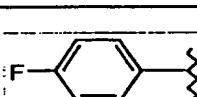
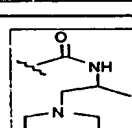
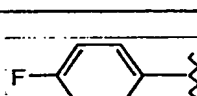
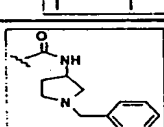
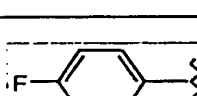
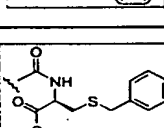
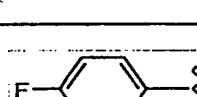
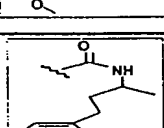

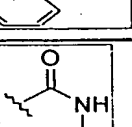

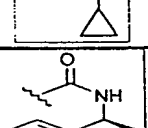
SUBSTITUTE SHEET (RULE 26)

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2325			41	382	383
B-2326			71	440	441
B-2327			36	464	465
B-2328			32	467	468
B-2329			34	465	466
B-2330			26	364	365
B-2331			38	464	465
B-2332			33	483	484
B-2333			36	378	379

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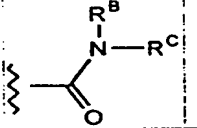
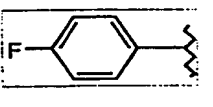
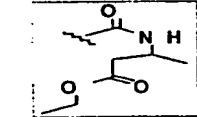
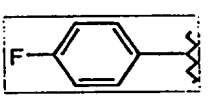
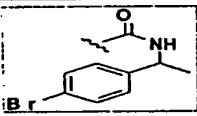
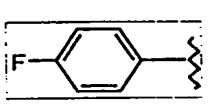
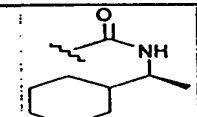
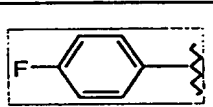
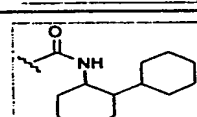
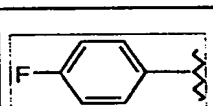
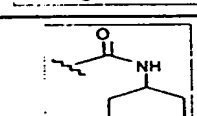
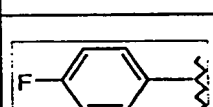
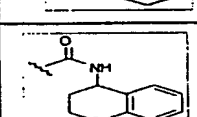
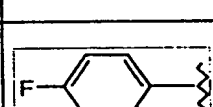
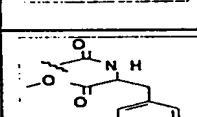
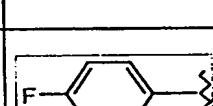
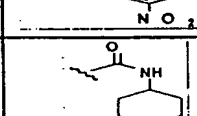
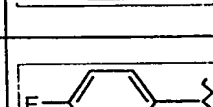
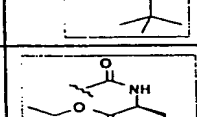
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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2334			44	428	429
B-2335			27	406	407
B-2336			41	428	429
B-2337			27	423	424
B-2338			33	469	470
B-2339			52	518	519
B-2340			64	442	443
B-2341			41	350	351
B-2342			34	414	415

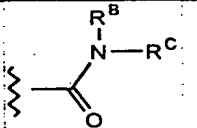
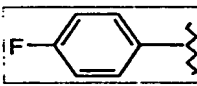
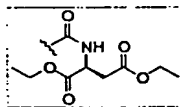

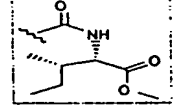
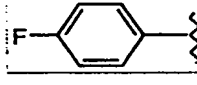
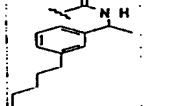
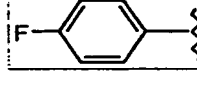
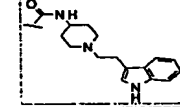
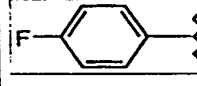
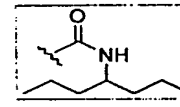
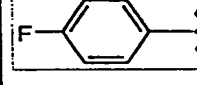
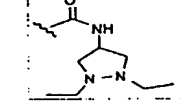
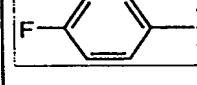
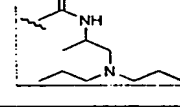
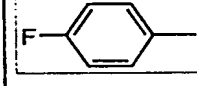
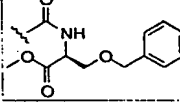
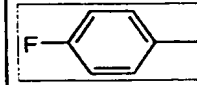
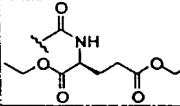
SUBSTITUTE SHEET (RULE 26)



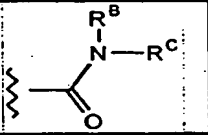
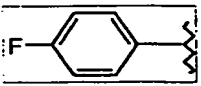
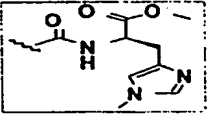
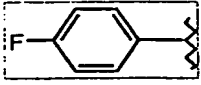
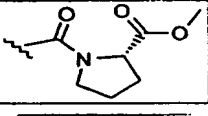
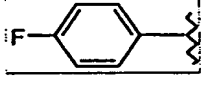
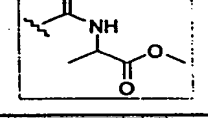
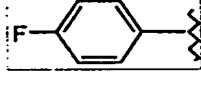
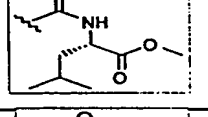
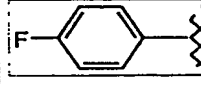
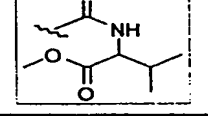
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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2343			29	424	425
B-2344			33	492	493
B-2345			30	420	421
B-2346			35	474	475
B-2347			34	392	393
B-2348			51	458	459
B-2349			73	517	518
B-2350			22	448	449
B-2351			64	486	487

SUBSTITUTESHEET (RULE 26)

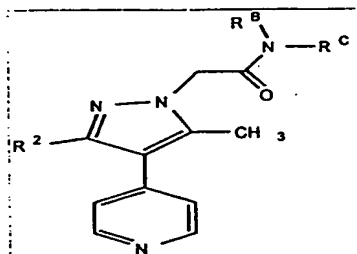
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B-2352			41	482	483
B-2353			57	438	439
B-2354			63	484	485
B-2355			28	536	537
B-2356			29	408	409
B-2357			41	436	437
B-2358			41	451	452
B-2359			57	502	503
B-2360			46	496	497

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2361			13	476	477
B-2362			46	493	494
B-2363			57	396	397
B-2364			61	438	439
B-2365			72	424	425

SUBSTITUTE SHEET (RULE 26)

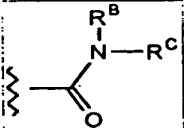

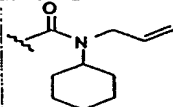
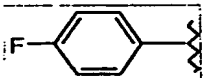
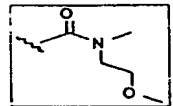
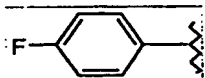
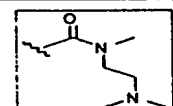
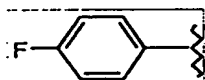
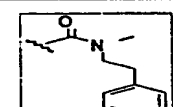
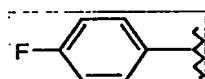
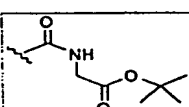
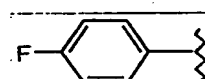
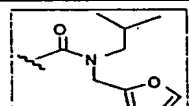
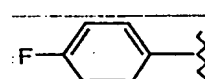
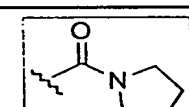
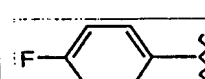
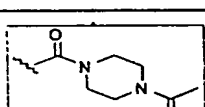
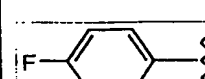
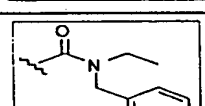
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	R <sup>2</sup>		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2366			34	380	381
B-2367			52	480	481
B-2368			35	407	407
B-2369			31	435	436
B-2370			33	414	415
B-2371			28	366	367
B-2372			37	422	423

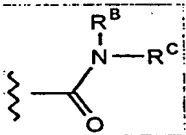
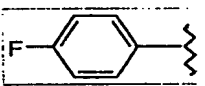
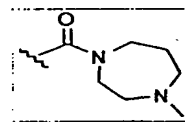
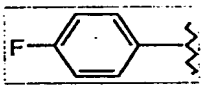
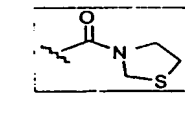
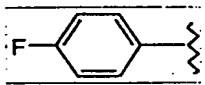
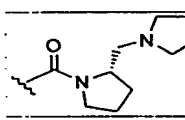
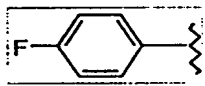
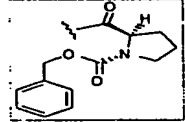
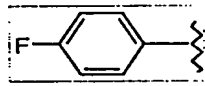
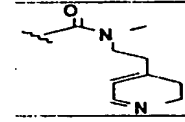

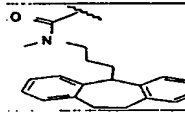
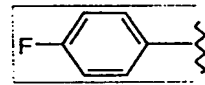
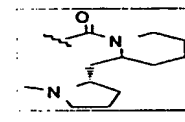
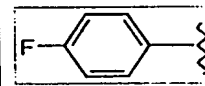
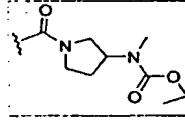
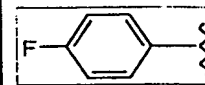
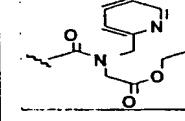
SUBSTITUTE SHEET (RULE 26)

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2373			50	432	433
B-2374			29	382	383
B-2375			35	395	396
B-2376			36	428	429
B-2377			68	438	439
B-2378			55	446	447
B-2379			33	364	365
B-2380			51	421	422
B-2381			52	429	430

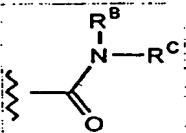
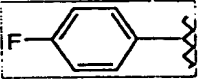
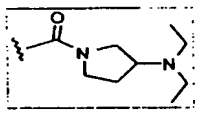
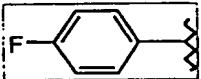
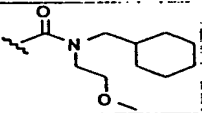
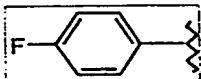
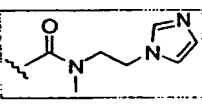
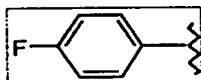
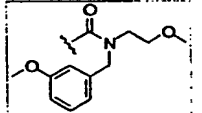
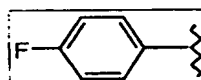
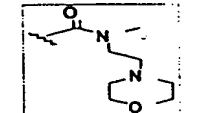
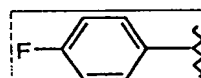
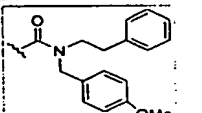
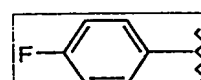
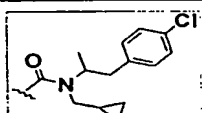
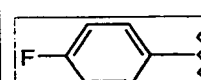
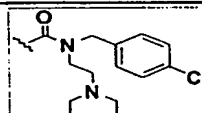
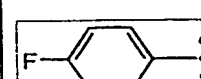
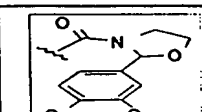
SUBSTITUTESHEET (RULE 20)

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2382			48	407	408
B-2383			53	382	383
B-2384			38	447	448
B-2385			59	498	450
B-2386			45	429	430
B-2387			74	558	-
B-2388			53	475	-
B-2389			33	493	494
B-2390			53	487	488

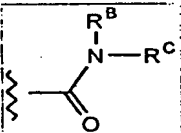
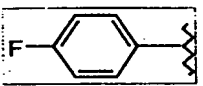
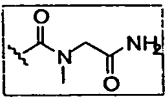
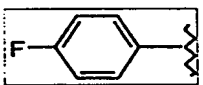
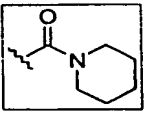
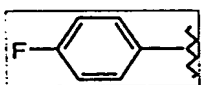
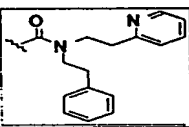
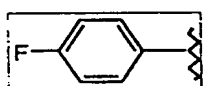
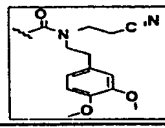
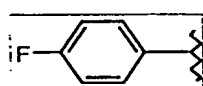
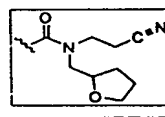
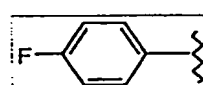
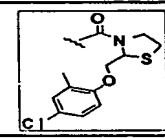
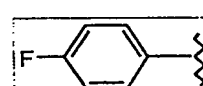
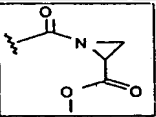
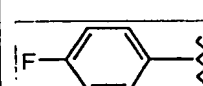
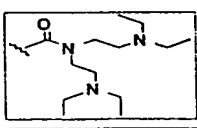
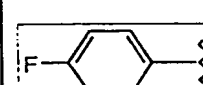
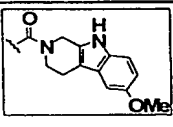
SUBSTITUTE SHEET (RULE 26)

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2391			30	435	436
B-2392			57	464	465
B-2393			50	418	419
B-2394			65	488	489
B-2395			59	437	438
B-2396			34	534	535
B-2397			32	516	517
B-2398			81	533	534
B-2399			55	502	-

SUBSTITUTE SHEET (RULE 26)

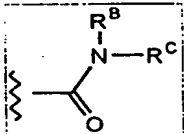
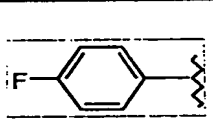
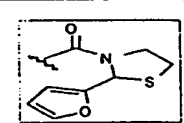
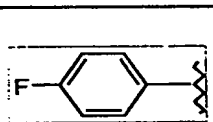
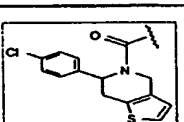
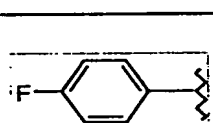
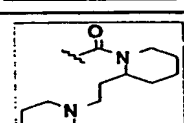
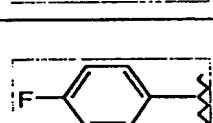
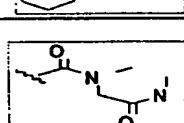
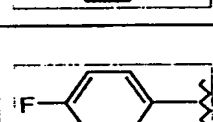
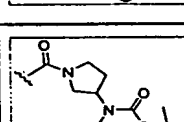
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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2400			34	381	382
B-2401			32	378	379
B-2402			71	519	520
B-2403			68	527	528
B-2404			62	447	448
B-2405			71	536	537
B-2406			47	394	395
B-2407			65	508	509
B-2408			34	495	496

SUBSTITUTE SHEET (RULE 26)

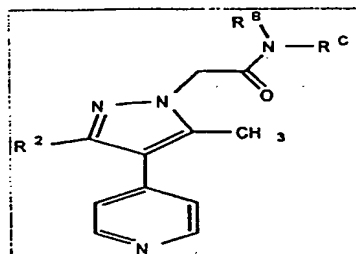


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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2409			47	448	449
B-2410			73	542	543
B-2411			81	489	490
B-2412			54	409	410
B-2413			37	493	494

SUBSTITUTE SHEET (RULE 26)

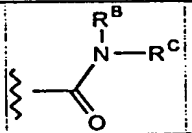
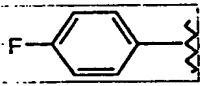
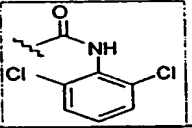
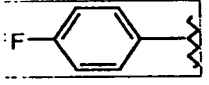
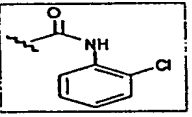
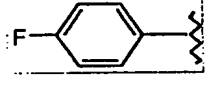
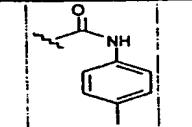
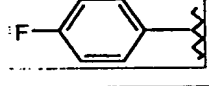
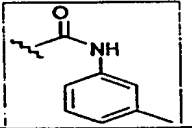
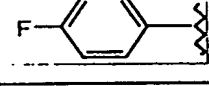
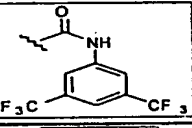
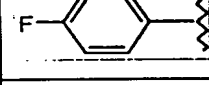
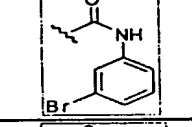
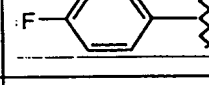
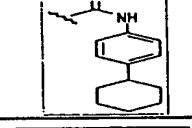
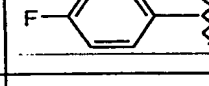
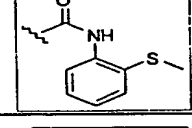
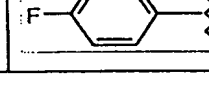
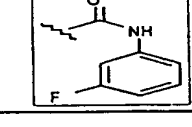
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	R <sup>2</sup>		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2414			14	473	474
B-2415			19	421	422
B-2416			13	386	387
B-2417			29	414	415
B-2418			6	420	421
B-2419			10	454	-
B-2420			5	442	443

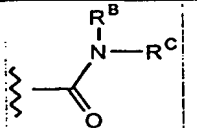
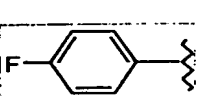
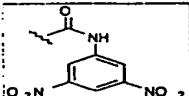
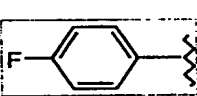
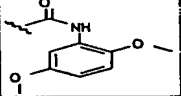
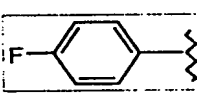
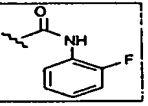
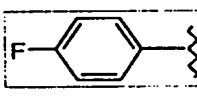
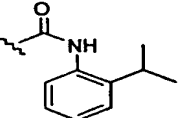
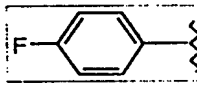
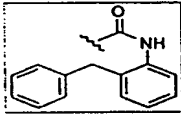
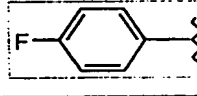
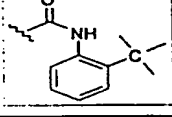
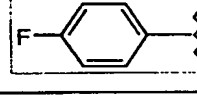
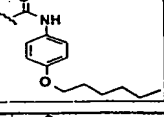
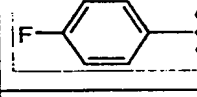
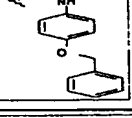
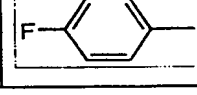
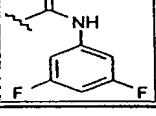
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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2421			28	454	455
B-2422			47	420	421
B-2423			53	400	401
B-2424			15	400	401
B-2425			18	522	523
B-2426			38	464	465
B-2427			26	468	469
B-2428			22	432	433
B-2429			41	404	405

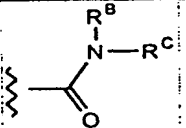
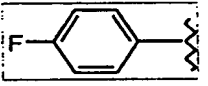
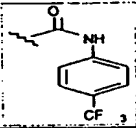
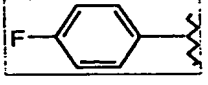
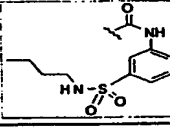
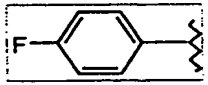
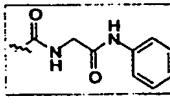
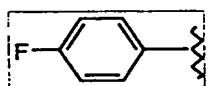
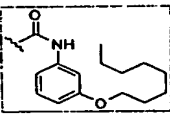
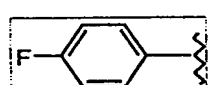
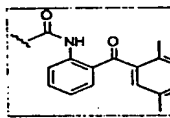
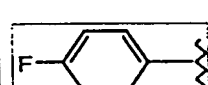
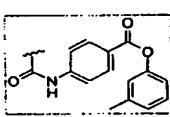
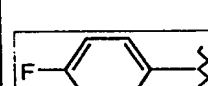
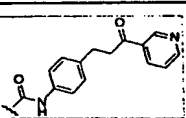
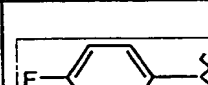
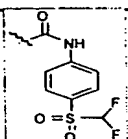

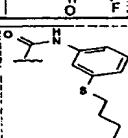
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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2430			15	476	477
B-2431			6	446	447
B-2432			37	404	405
B-2433			8	428	429
B-2434			13	476	477
B-2435			23	442	443
B-2436			5	486	487
B-2437			4	492	493
B-2438			58	422	423

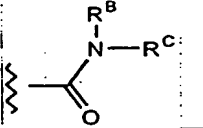
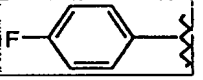
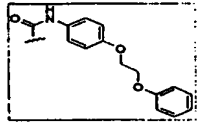
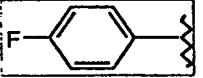
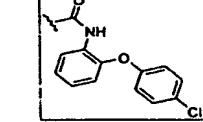
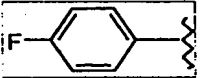
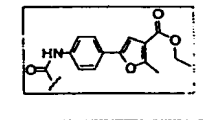
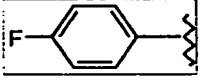
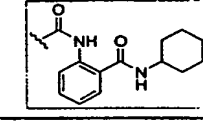
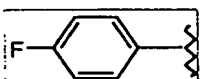
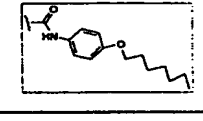
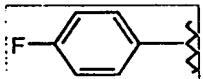
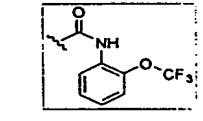
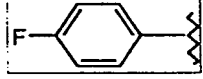
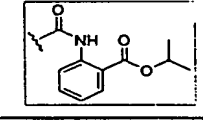
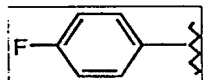
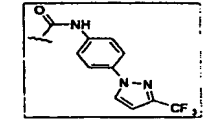

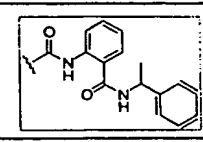
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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2439			12	454	455
B-2440			8	521	522
B-2441			6	443	444
B-2442			37	514	515
B-2443			15	518	-
B-2444			52	520	-
B-2445			33	517	518
B-2446			70	500	501
B-2447			56	488	489

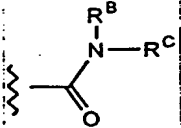
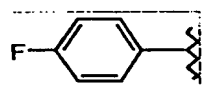
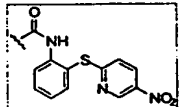
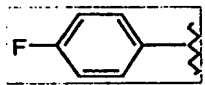
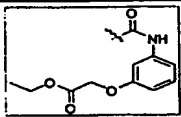

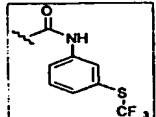
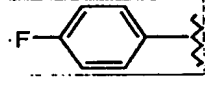
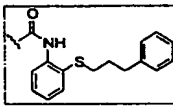
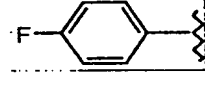
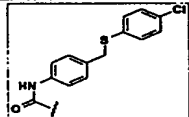
SUBSTITUTE SHEET (RULE 26)

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2448			51	522	523
B-2449			19	512	513
B-2450			16	538	539
B-2451			71	511	512
B-2452			71	500	501
B-2453			61	470	-
B-2454			15	472	473
B-2455			39	520	-
B-2456			51	533	534

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	$R^2$		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2457			55	540	-
B-2458			22	488	489
B-2459			8	486	487
B-2460			13	534	535
B-2461			13	542	-

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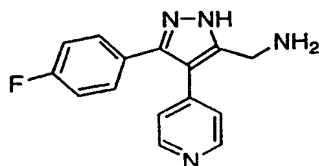
5

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## Example C-1

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## 5-AMINOMETHYL-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



20        1-(4-fluorophenyl)-2-(4-pyridyl)-1-ethanone.        4-  
picoline (40 g, 0.43 mol) was added to a LiHMDS solution  
(0.45 mol, 450 mL of a 1.0 M solution in THF) over 30  
minutes at room temperature (a slight exotherm was  
observed) The resulting solution was stirred for 1 h.  
25 This solution was added to ethyl 4-fluorobenzoate (75.8  
g, 0.45 mol, neat) over 1 h. The mixture was stirred  
overnight (16 h). Water (200 mL) was added and the  
mixture was extracted with EtOAc (2x200 mL). The organic  
layer was washed with brine (1x200 mL) and dried over



Na<sub>2</sub>SO<sub>4</sub>. The organic layer was filtered and the solvent was removed to leave oily solid. Hexane was added to the oil and the resulting solid was filtered and washed with hexane (cold). A yellow solid was isolated (50 g, 54%):  
5 <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.58 (d, J = 5.7 Hz, 2H), 8.02 (dd, J = 5.5, 8.0, 2H), 7.12-7.21 (m, 4H), 4.23 (s, 2H); <sup>19</sup>F NMR (CDCl<sub>3</sub>) δ -104.38 (m); LC/MS, t<sub>r</sub> = 2.14 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C), M+H = 216; High Resolution MS Calcd for  
10 C<sub>23</sub>H<sub>20</sub>N<sub>4</sub>O<sub>2</sub>F (M+H): 216.0825. Found: 216.0830 (Δ mmu = 0.5).

**N-benzyloxycarbonyl-5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole.** A 3L round bottom flask  
15 fitted with a mechanical stirrer, N<sub>2</sub> inlet and an addition funnel was charged with 557 mL (0.56 mol) of 1 M t-BuOK in THF and 53 mL (0.56 mol) of t-BuOH. The ketone, 1 (60 g, 0.28 mol) was dissolved in 600 mL of THF and added to the stirred mixture at room temperature. A yellow  
20 precipitate formed and the mixture was stirred for 1 h. N-benzyloxycarbonyl-glycinyll N-hydroxysuccinimide (128.6 g, 0.42 mol) was dissolved in 600 mL of THF and added dropwise at r.t. over 1h. The mixture was stirred for another 5 minutes and 150 mL of water was added. the pH  
25 was adjusted to 6.7 with 70 mL of AcOH. Hydrazine monohydrate (41 mL in 100 mL of water) was added via an addition funnel. The mixture was stirred for 1 h and was diluted with 500 mL of water and 500 mL of ethyl acetate. The biphasic mixture was transferred to a sep funnel and  
30 the layers were separated. The aqueous layer was extracted with EtOAc (3x300 mL). The organic layer was

dried ( $\text{Na}_2\text{SO}_4$ ), filtered and evaporated to leave 157 g of a crude reddish oil.

The oil was suspended in  $\text{CH}_2\text{Cl}_2$  and filtered to remove any insoluble material (DCU, hydrazone of the monoketone). The solution was split into two portions and each portion was chromatographed (Biotage 75L, 3% EtOH/ $\text{CH}_2\text{Cl}_2$  then 6% EtOH/ $\text{CH}_2\text{Cl}_2$ ). The appropriate fractions were concentrated (some contamination from the monoketone and the hydrazone) from each portion to leave a yellow solid. The solid was suspended in ethyl acetate and heated to boiling for 10 minutes. The solution was allowed to cool to R.T. overnight. The precipitate was filtered to give 30 g of a white solid (27% yield of 2):  $^1\text{H}$  NMR ( $\text{DMF-d}_7$ )  $\delta$  13.36 (s, 1H), 8.57 (d,  $J$  = 5.8 Hz, 2H), 7.16-7.52 (m, 11H), 5.11 (s, 2H), 4.48 (d,  $J$  = 5.4 Hz, 2H);  $^{19}\text{F}$  NMR ( $\text{DMF-d}_7$ )  $\delta$  -114.9 (m), -116.8 (m) (split fluorine signal is due to the pyrazole tautomers); LC/MS,  $t_r$  = 3.52 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C),  $M+H$  = 403; High Resolution MS Calcd for  $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2\text{F}$  ( $M+H$ ): 403.1570. Found: 403.1581 ( $\Delta$  mmu = 1.1).

**5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl)**

**pyrazole.** To a 1L Parr bottle was added 7 g (17.4 mmol) of 2 and 180 mL of MeOH and 90 mL of THF to give a clear solution. The bottle was purged with nitrogen and 1.5 g of 10% Pd/C (wet Degussa type E101) was added. The Parr bottle was pressured to 40 psi ( $\text{H}_2$ ) and was agitated. Hydrogen uptake was 5 psi after 5 h. The bottle was repressured to 42 psi and was agitated overnight. The bottle was purged with  $\text{N}_2$  and was filtered through Celite. The Celite was washed with MeOH (3x50 mL) and

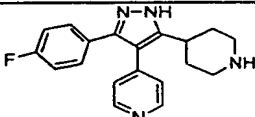
the filtrate was concentrated to give 4.5 g of an off-white solid (94%).  $^1\text{H}$  NMR (DMSO- $d_6$ )  $\delta$  8.52 (d,  $J$  = 4.63 Hz, 2H), 7.36 (dd,  $J$  = 5.64, 8.1 Hz, 2H), 7.16-7.30 (m, 4H), 3.79 (s, 2H);  $^{19}\text{F}$  NMR (DMSO- $d_6$ )  $\delta$  -114.56 (m); LC/MS,  $t_r$  = 1.21 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C),  $M+H$  = 269 m/z; High Resolution MS Calcd for  $\text{C}_{15}\text{H}_{14}\text{N}_4\text{F}$  ( $M+H$ ): 269.1202. Found: 269.1229 ( $\Delta$  mmu = 2.7).

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The following pyridylpyrazoles (C-2 through C-21, Table C-1) were prepared according to the experimental procedure described above for example C-1.

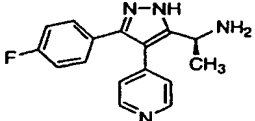
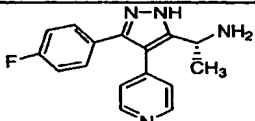
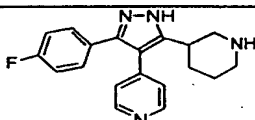
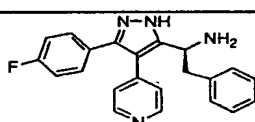
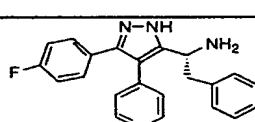
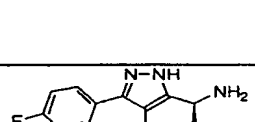
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Table C-1.

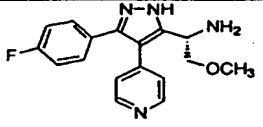
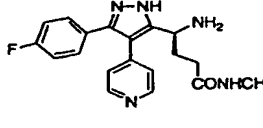
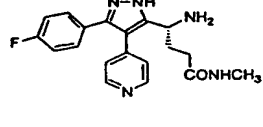
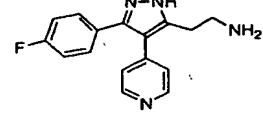
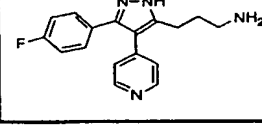
Example No.	Structure	MW, $M + H$ Calculated Found	$^1\text{H}$ NMR (solvent), ppm
C-2		323.1672 323.1670	(DMF- $d_7$ ): 8.77 (t, $J$ = 4.4 Hz, 2H), 7.60 (m, 2H), 7.44 (t, $J$ = 4.4 Hz, 2H), 7.35 (m, 2H), 3.22 (bd, 2H), 3.01 (septet, $J$ = 5.3 Hz, 1H), 2.74 (m, 2H), 1.95 (m, 4H)

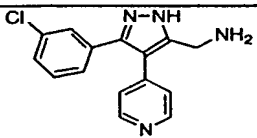
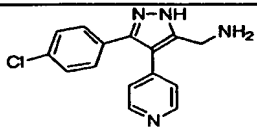
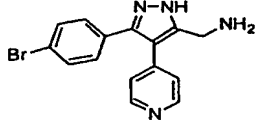
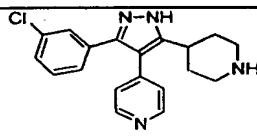
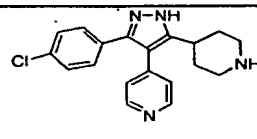
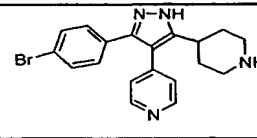
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C-3		282.127 (M) 282.1245 (M, EI)	(DMF-d <sub>7</sub> ): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.34 (m, 2H), 4.40-4.37 (m, 1H), 1.56 (br s, 3H)
C-4		282.127 (M) 282.1147 (M, EI)	(DMF-d <sub>7</sub> ): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.35 (m, 2H), 4.40-4.37 (m, 1H), 1.57 (br s, 3H)
C-5		323.1672 323.1687	(DMSO-d <sub>6</sub> ): 8.56 (br, 2H), 7.32 (m, 2H), 7.18 (m, 4H), 2.91 (m, 2H), 2.71 (m, 2H) 1.88 (m, 1H), 1.65 (m, 2H), 1.40 (m, 2H)
C-6		359 359	(DMSO-d <sub>6</sub> ): 8.46 (d, J = 4.6 Hz, 2H), 7.32-7.13 (m, 7H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.95 (m, 2H)
C-7		359 359	(DMSO-d <sub>6</sub> ): 8.46 (d, J = 5.4 Hz, 2H), 7.32-7.28 (m, 2H), 7.20-7.12 (m, 5H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.94 (m, 2H)
C-8		313.1465 313.1492	(DMSO-d <sub>6</sub> ): 13.83 (bs, 1H), 8.61 (d, J = 5.7 Hz, 2H), 8.33 (bs, 1H), 7.33 (m, 6H), 4.44 (m, 1H), 3.63 (m, 2H), 3.27 (s, 3H)

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C-9		313.1465 313.1457	(DMSO-d <sub>6</sub> ): 8.55 (dd, J = 1.5, 4.4 Hz, 2H), 7.37-7.32 (m, 2H), 7.26 (dd, J = 1.6, 4.4 Hz, 2H), 7.22-7.16 (m, 2H), 4.06 (t, J = 6.5 Hz, 1H), 3.49 (d, J = 6.6 Hz, 2H), 3.20 (s, 3H)
C-10		354 354	(DMSO-d <sub>6</sub> ): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-11		354 354	(DMSO-d <sub>6</sub> ): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-12		283.1359 283.1363	(DMSO-d <sub>6</sub> ): 8.53 (d, J = 5.0 Hz, 2H), 7.37-7.32 (m, 2H), 7.21-7.17 (m, 4H), 2.83 (d, J = 6.0 Hz, 2H), 2.77 (d, J = 6.0 Hz, 2H)
C-13		297.1515 297.1515	(DMSO-d <sub>6</sub> ): 8.53 (d, J = 5.4 Hz, 2H), 7.34 (dd, J = 5.8, 8.2 Hz, 2H), 7.18

			(dd, $J = 5.8, 9.8$ Hz, 4H), 2.68 (t, $J = 7.3$ Hz, 2H), 2.52 (m, 2H), 1.64 (m, 2H)
C-14		284.0829 284.0806	(CD <sub>3</sub> OD): 8.74 (br, 2H), 7.77 (br, 2H), 7.45-7.58 (m, 3H), 7.30-7.40 (m, 1H), 4.43 (s, 2H)
C-15		285 285	(DMSO-d <sub>6</sub> ): 8.53 (br, 2H), 7.56 (br, 2H), 7.26 (m, 4H), 3.75 (br, 2H)
C-16		329, 331 329, 331	(DMSO-d <sub>6</sub> ): 8.53 (d, $J =$ 4.4 Hz, 2H), 7.42 (d, $J =$ 7.9 Hz, 2H), 7.34 (d, $J =$ 8.5 Hz, 2H), 7.24 (d, $J =$ 4.6 Hz, 2H), 3.76 (bs, 2H)
C-17		339 339	(DMSO-d <sub>6</sub> ): 8.53 (t, $J =$ 4.3 Hz, 2H), 7.33 (m, 3H), 7.19 (t, $J = 4.6$ Hz, 2H), 7.14 (d, $J = 7.3$ Hz, 1H), 3.23 (m, 2H), 2.88, (m, 3H), 1.92, (m, 3H), 1.70 (m, 1H)
C-18		339 339	(DMSO-d <sub>6</sub> ): 8.57 (d, $J =$ 4.6 Hz, 2H), 7.41 (d, $J =$ 8.3 Hz, 2H), 7.29 (d, $J =$ 8.5 Hz, 2H), 7.20 (d, $J =$ 4.8 Hz, 2H), 3.18 (bd, 2H), 2.88 (m, 1H), 2.76 (m, 2H), 1.82 (br, 4H)
C-19		383, 385 383, 385	(DMSO-d <sub>6</sub> ): 8.56 (br, 2H), 7.52 (br, 2H), 7.14-7.29 (m, 4H), 2.99 (br, 2H),

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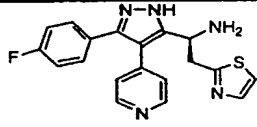
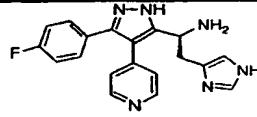
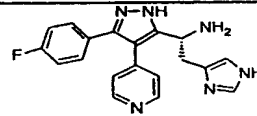
			2.71 (br, 1H), 2.51 (br, 2H), 1.68 (br, 4H)
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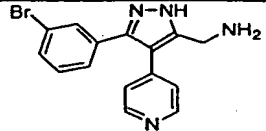
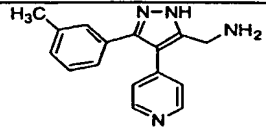
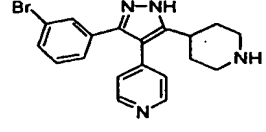
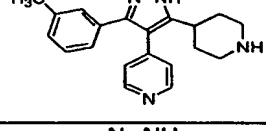
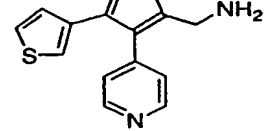
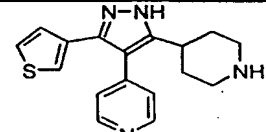
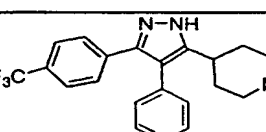
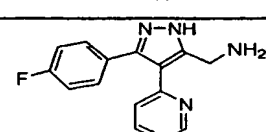
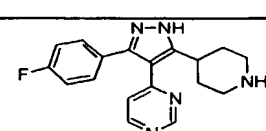
The following pyridylpyrazoles (C-22 through C-40, Table C-2) are prepared utilizing the general schemes C-1 and C-2 and the experimental procedure described for example C-1 above.

Table C-2

Cmpd. No.	Structure
C-22	
C-23	
C-24	

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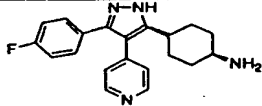
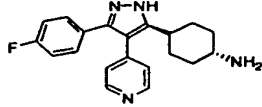
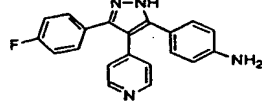
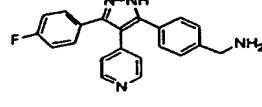
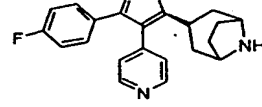
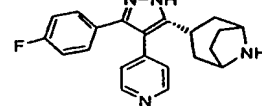
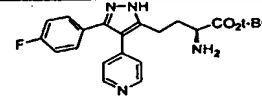
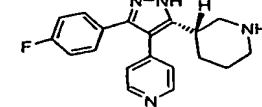
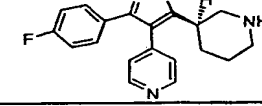
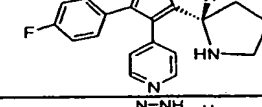
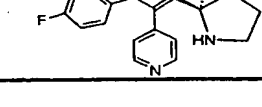
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C-25	
C-26	
C-27	
C-28	
C-29	
C-30	
C-31	
C-32	
C-33	

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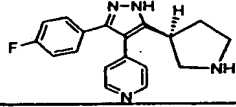
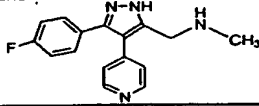
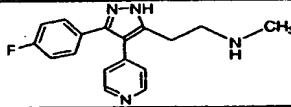
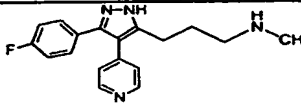


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C-34	
C-35	
C-36	
C-37	
C-38	
C-39	
C-40	
C-41	
C-42	
C-43	
C-44	

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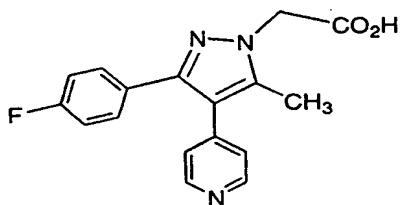
650

C-45	
C-46	
C-47	
C-48	

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**Example C-49**

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**Step A**

The pyrazole (2.60 g, 10.3 mmol) from **example 4** was suspended in 52 mL of dichloroethane and 52 mL of 2.5 M

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NaOH. Tetrabutylammonium hydroxide (0.5 mL of a 1 M aqueous solution) was added to the stirred mixture. To this mixture was added t-butyl bromoacetate (2.10 g, 10.8 mmol). The reaction mixture was stirred at room temperature for 4 h. The mixture was poured onto 200 mL of CH<sub>2</sub>Cl<sub>2</sub> and 200 mL of H<sub>2</sub>O. The phases were separated and the organic phase was washed with water (1x100 mL) and brine (1x100 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and was filtered. The solvent was removed to leave an off-white solid. This solid was triturated with hexane and the resulting solid isolated by filtration. The solid was washed with hexane to leave 3.4 g of a white solid (90%).

15

**Step B**

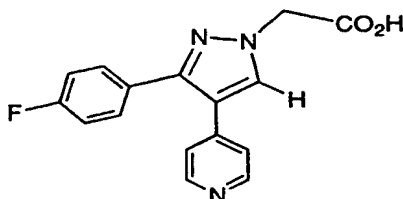
The alkylated pyrazole (3.7 g, 10.1 mmol) from Step A was treated with 57 mL of 4 N HCL in dioxane. The solution was stirred at room temperature for 4 h. The solvent was removed under reduced pressure and the residue was dissolved in THF. The solution was treated with propylene oxide (10.3 mmol) and was stirred for 1h at room temperature. The solvent was removed to leave an oil. The residual solvent was chased with several portions of EtOH. The resulting solid was triturated with Et<sub>2</sub>O and the title compound Example C-49 was isolated by filtration to afford 3.0 g of an off-white solid (95%). Mass spec: M+H calcd: 312; found 312. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): 8.81 (d, J = 6.4 Hz, 2H), 7.73 (d, J =

**SUBSTITUTESHEET (RULE 26)**

652

5.8 Hz, 2H), 7.40 (m, 2H), 7.23 (t,  $J = 8.5$  Hz, 1H), 5.16 (s, 2H), 2.40 (s, 3H).

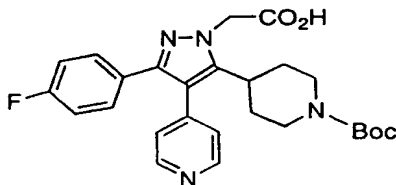
5

**Example C-50**

According to the procedure described above in Example C-  
10 49, Example C-50 was also prepared starting from 4-[3-(4-fluorophenyl)-1H-pyrazole-4-yl]pyridine. Mass spec:  $M+H$  calcd: 298; found 298.  $^1H$  NMR (DMSO- $d_6$ ): 8.75 (d,  $J = 6.4$  Hz, 2H), 8.68 (s, 1H), 7.78 (d,  $J = 6.6$  Hz, 2H), 7.52 (dd,  $J = 5.4, 8.5$  Hz, 2H), 7.31 (t,  $J = 8.9$  Hz, 2H),  
15 5.16 (s, 2H).

**Example C-51**

20

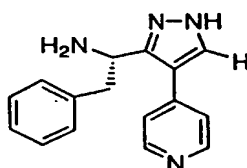


Starting with the N-Boc-piperidinyl analog of Example C-2, Example C-51 is also prepared according to the methods described in Scheme C-1.

**SUBSTITUTESHEET (RULE 26)**

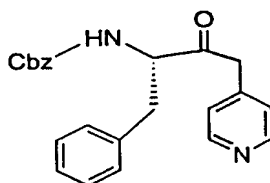
## Example C-52

5



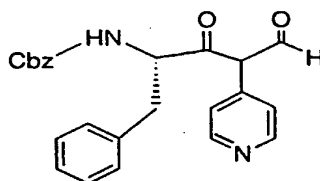
Step A: Picoline is treated with a base chosen from but not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH in an organic solvent such as THF, ether, t-BuOH or dioxane from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. The picoline solution is then added to a solution of N-Cbz-(L)-phenylalaninyl N-hydroxysuccinimide. The reaction is allowed to stir from 30 minutes to 48 hours during which time the temperature may range from -20 °C to 120 °C. The mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the pyridyl monoketone is isolated as a crude solid which could be purified by crystallization and/or chromatography.

20



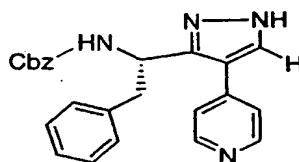
25 Step B: A solution of the pyridyl monoketone in ether, THF, tBuOH, or dioxane is added to a base chosen from but

not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH contained in hexane, THF, ether, dioxane, or tBuOH from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. Formyl acetic anhydride is then added as a solution in THF, ether, or dioxane to the monoketone anion while the temperature is maintained between -50 °C and 50 °C. The resulting mixture is allowed to stir at the specified temperature for a period of time from 5 minutes to several hours. The resulting pyridyl diketone intermediate is utilized without purification in Step C.



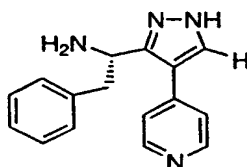
Step C: The solution containing the pyridyl diketone is quenched with water and the pH is adjusted to between 4 and 8 utilizing an inorganic or organic acid chosen from HOAc, H<sub>2</sub>SO<sub>4</sub>, HCl, or HNO<sub>3</sub>. The temperature during this step is maintained between -20 °C and room temperature. Hydrazine or hydrazine hydrate is then added to the mixture while maintaining the temperature between -20 °C and 40 °C for a period of 30 minutes to several hours. The mixture is then poured into water and extracted with an organic solvent. The N-Cbz-protected pyridyl pyrazole is obtained as a crude solid which is purified by chromatography or crystallization.

655



## 5 Step: D

The CBZ protecting group is cleaved using hydrogen gas under pressure and Pd-C in an alcohol solvent, affording scaffold C-52 after filtration and concentration.



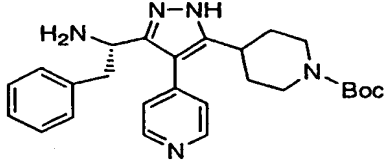
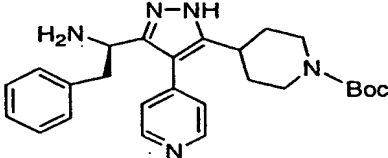
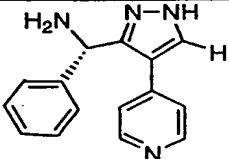
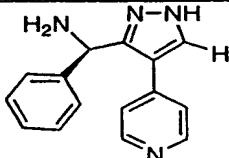
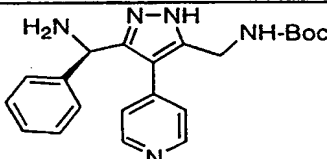
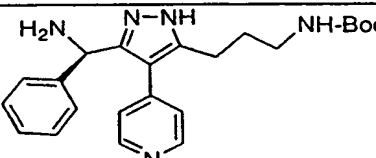
10

- 15 The following compounds C-53 through C-59 in Table C-3 are prepared according to the general procedure described above for the preparation of C-52.

Table C-3

Example No.	Structure
C-53	

656

C-54	
C-55	
C-56	
C-57	
C-58	
C-59	

**Example C-60****5 Step A:**

A Boc protected pyridylpyrazole is treated with benzaldehyde in methylene chloride at room temperature in

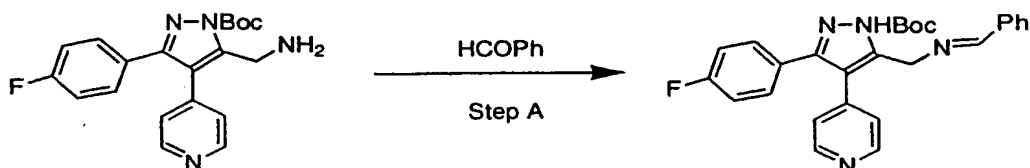
**SUBSTITUTE SHEET (RULE 26)**



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the presence of a drying agent for a period of time ranging from 1-24 h. Solvent is then evaporated and the resulting imine is used in step B without further purification.

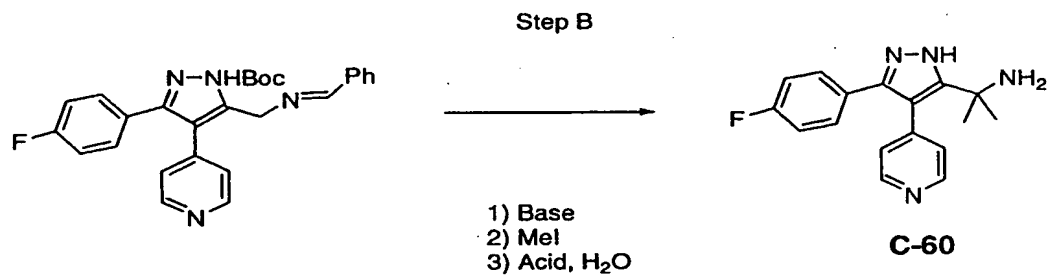
5

**Step B:**

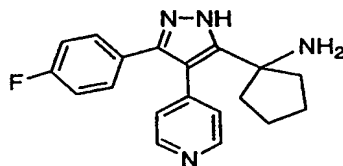
The pyridylpyrazole imine is dissolved in THF and stirred under nitrogen at temperatures ranging from -78 to -20 °C. A base such as LDA, n-BuLi, or LiHMDS is added dropwise to the mixture which is then stirred for an additional 10 minutes to 3 h. Two equivalents of a methyl iodide are then added to the mixture and stirring is continued for several hours. The mixture is then quenched with acid and allowed to warm to room temperature and stirred several hours until cleavage of the Boc and the imine functions is complete. The pH is adjusted to 12 and then the mixture is extracted with an organic solvent, which is dried and evaporated. The crude pyridylpyrazole is then crystallized and/or chromatographed to give purified C-60.

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5

**Example C-61**

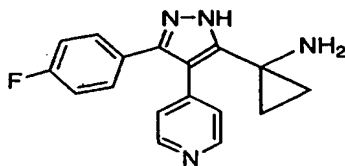
10 Example C-61 is prepared according to the method described in example C-60, substituting 1,4-dibromobutane for methyl iodide.

15

20

**Example C-62****SUBSTITUTESHEET (RULE 26)**

659



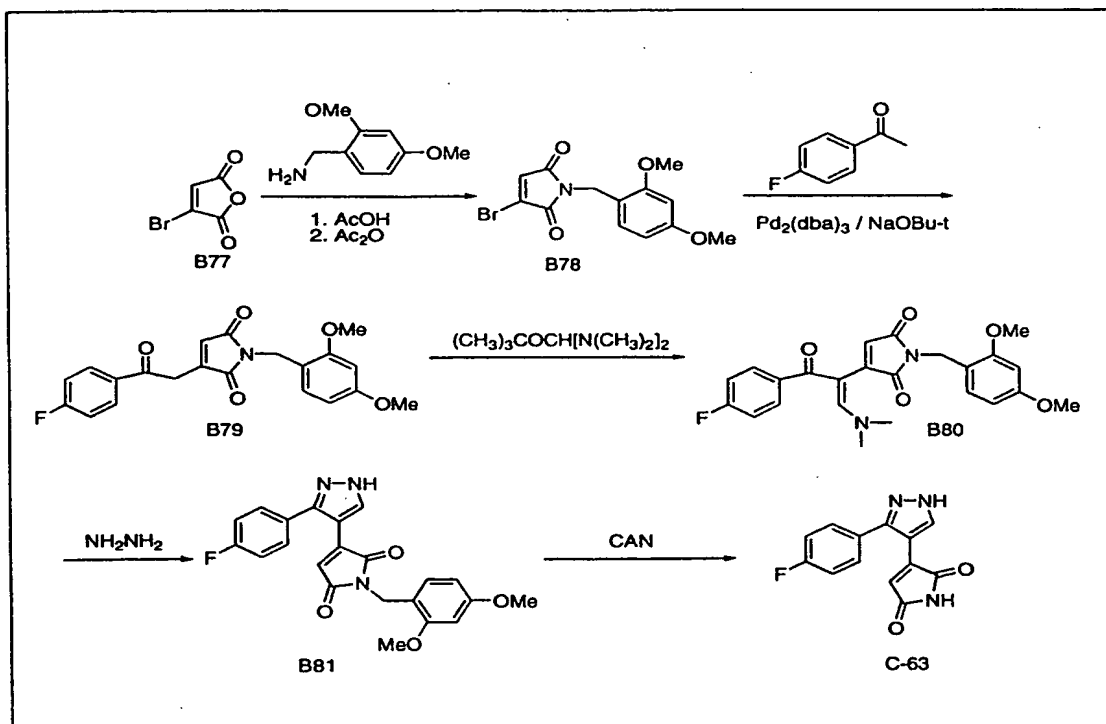
Example C-62 is prepared according to the method described in example C-60, substituting 1,3-dibromoethane for methyl iodide.

5

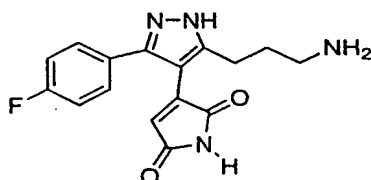
### Example C-63

The synthesis of compound C-63 starts with the  
10 condensation reaction of bromomaleic anhydride B77 with  
2, 4-dimethoxybenzylamine in acetic acid and acetic  
anhydride. The maleimide B78 is then treated with 4'-  
fluoroacetophenone in the presence of catalytic amount  
Pd<sub>2</sub>(dba)<sub>3</sub> and sodium t-butoxide to form the  
15 fluoroacetophenone substituted maleimide B79. B79 is  
then treated with tert-butoxybis(dimethylamino)methane to  
yield the α-ketoenamine B80. The α-ketoenamine B80 is  
condensed with hydrazine to form the N-protected  
maleimide pyrazole B81. The 2,4-dimethoxybenzyl group is  
20 cleaved with ceric ammonium nitrate (CAN) to give the  
title compound C-63.

660

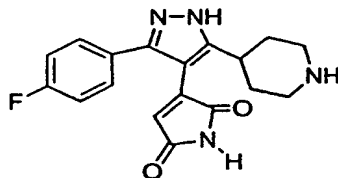
**Example C-64**

5



Using the method described in Schemes C-6 and C-7,  
 10 Example 64 is prepared.

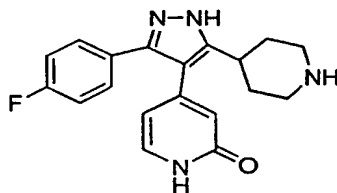
661

**Example C-65**

5

Using the method described in Schemes C-6 and C-7, Example 65 is prepared.

10

**Example C-66**

15

Using the method described in Schemes C-6 and C-7, Example C-66 is synthesized, substituting N-2,4-dimethoxybenzyl-4-bromopyridone for **B78**.

20

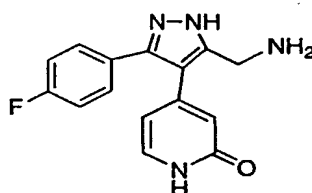
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**SUBSTITUTESHEET (RULE 20)**

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**Example C-67**

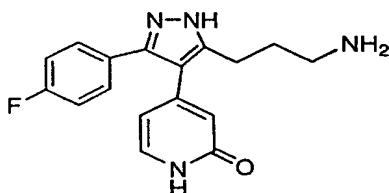
5



Using the method described in Schemes C-6 and C-7, Example C-67 is synthesized, substituting N-2,4-dimethoxybenzyl-4-bromopyridone for **B78**, and substituting  
10 N-Boc-glycyl N-hydroxysuccinimide for **B82**.

**Example C-68**

15

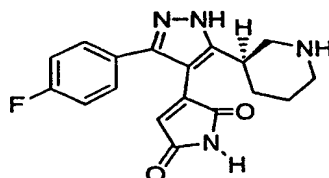


Using the method described in Schemes C-6 and C-7, Example C-68 is synthesized, substituting N-2,4-dimethoxybenzyl-4-bromopyridone for **B78**.  
20

25

**SUBSTITUTESHEET (RULE 26)**

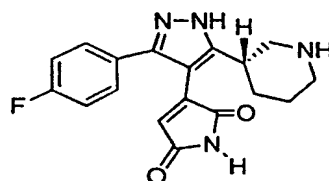
663

**Example C-69**

5

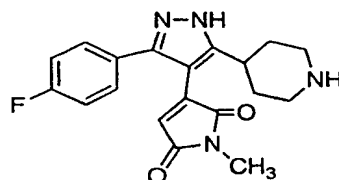
Using the method described in Schemes C-6 and C-7, Example 69 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

10

**Example C-70**

15 Using the method described in Schemes C-6 and C-7, Example 70 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

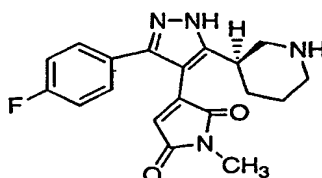
20

**Example C-71****SUBSTITUTESHEET (RULE 26)**

664

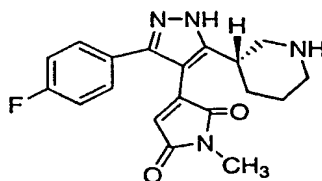
Using the method described in Schemes C-6 and C-7, Example 71 is prepared, substituting N-methyl-3-bromomaleimide for **B78**.

5

**Example C-72**

10 Using the method described in Schemes C-6 and C-7, Example 72 is prepared, substituting N-methyl-3-bromomaleimide for **B78**, and substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

15

**Example C-73**

20 Using the method described in Schemes C-6 and C-7, Example 73 is prepared, substituting N-methyl-3-bromomaleimide for **B78** and substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

25

**SUBSTITUTE SHEET (RULE 26)**



Biological data from compounds of Examples B-0001 through B-1573 and of Examples B-2270 through B-2462 are shown in the following tables.

In vitro P38-alpha kinase inhibitory data are shown in the column identified as:

"P38 alpha kinase IC<sub>50</sub>, uM or % inhib @ conc. (uM)"

10

In vitro whole cell assay for measuring the ability of the compounds to inhibit TNF production in human U937 cells stimulated with LPS are shown in the column identified as:

15

"U937 Cell IC<sub>50</sub>, uM or % inhib @ conc., (uM)"

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the mouse is shown in the column identified as:

20

"Mouse LPS Model, % TNF inhib @ dose @ predose time"

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time indicates the number of hours before LPS challenge when the compound is administered.

25

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the rat is shown in the column identified as:

30

"Rat LPS Model, % TNF inhib @ dose @ predose time"

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time

666

indicates the number of hours before LPS challenge when the compound is administered.

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Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0001	53.0%@1.0uM	40.0% @1.0uM		
B-0002	71.0%@1.0uM	28.0%@10.0uM		
B-0003	70.0%@1.0uM	76.0% 10.0uM		
B-0004	80.0%@1.0uM	4.61uM		
B-0005	95.0%@1.0uM	2.97uM		
B-0006	82.0%@1.0uM	80%@10.0uM		
B-0007	74.0%@1.0uM	85.0%@10.0uM		
B-0008	42.0%@1.0uM	65.0%@10.0uM		
B-0009	0.04 uM	0.72uM		
B-0010	0.52 uM	0.65uM		
B-0011	0.03 uM	4.47uM		
B-0012	30.0%@1.0uM	44.0% @1.0uM		
B-0013	70.0%@1.0uM	84.0%@10.0uM		
B-0014	79.0%@1.0uM	80.0%@10.0uM		
B-0015	82.0%@1.0uM	80.0%@10.0uM		
B-0016	94.0%@1.0uM	3.98uM		
B-0017	56.0%@1.0uM	79.0%@10.0uM		
B-0018	60.0%@1.0uM	59.0%@10.0uM		
B-0019	84.0%@1.0uM	100.0%@10.0uM		
B-0020	73.0%@1.0uM	81.0%@10.0uM		
B-0021	68.0%@1.0uM	76.0%@10.0uM		
B-0022	69.0%@1.0uM	44.0@1.0uM		
B-0023	90.0%@1.0uM	77.0%@10.0uM		
B-0024	94.0%@1.0uM	52.0%@1.0uM		
B-0025	89.0%@1.0uM	79.0%@10.0uM		
B-0026	96.0%@1.0uM	3.27uM		
B-0027	94.0%@1.0uM	11.0uM		
B-0028	69.0%@1.0uM	45.0%@10.0uM		
B-0029	91.0%@1.0uM	58.0%@10.0uM		
B-0030	92.0%@1.0uM	75.0%@10.0uM		
B-0031	94.0%@1.0uM	100.0%@10.0uM		
B-0032	94.0%@1.0uM	78.0%@10.0uM		
B-0033	97.0%@1.0uM	10.0uM		
B-0034	95.0%@1.0uM	10.0uM		
B-0035	94.0%@1.0uM	10.0uM		
B-0036	92.0%@1.0uM	8.24uM		
B-0037	91.0%@1.0uM	86.0%@10.0uM		
B-0038	71.0%@1.0uM	84.0%@10.0uM		
B-0039	89.0%@1.0uM	72.0%@10.0uM		
B-0040	93.0%@1.0uM	2.3uM		
B-0041	65.0%@1.0uM	66.0%@10.0uM		
B-0042	94.0%@1.0uM	2.76uM		

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Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0043	0.22 uM	0.54uM		
B-0044	0.14 uM	0.19uM		
B-0045	94.0%@1.0uM	1.01uM		
B-0046	96.0%@1.0uM	54.0%@1.0uM		
B-0047	94.0%@1.0uM	74.0%@10.0uM		
B-0048	94.0%@1.0uM	76.0%@10.0uM		
B-0049	88%@1.0uM	33.0%@1.0uM		
B-0050	73%@1.0uM	34.0%@1.0uM		
B-0051	3.3uM	2.15uM	47%@100mpk@-6h	79%@3mpk@-4h
B-0052	92%@1.0uM	15.0%@1.0uM		
B-0053	95%@1.0uM	34.0%@1.0uM		
B-0054	90%@1.0uM	30.0%@1.0uM		
B-0055	93%@1.0uM	>1.0uM		
B-0056	96%@1.0uM	21.0%@1.0uM		
B-0057	96%@1.0uM	29.0%@1.0uM		
B-0058	79%@1.0uM	18.0%@1.0uM		
B-0059	83%@1.0uM	35.0%@1.0uM		
B-0060	73%@1.0uM	22.0%@1.0uM		
B-0061	62%@1.0uM	27.0%@1.0uM		
B-0062	94%@1.0uM	36.0%@1.0uM		
B-0063	96%@1.0uM	40.0%@1.0uM		
B-0064	90%@1.0uM	4.0%@1.0uM		
B-0065	83%@1.0uM	21.0%@1.0uM		
B-0066	94%@1.0uM	28.0%@1.0uM		
B-0067	91%@1.0uM	1.0%@1.0uM		
B-0068	72%@1.0uM	22.0%@1.0uM		
B-0069	96%@1.0uM	37.0%@1.0uM		
B-0070	92%@1.0uM	30.0%@1.0uM		
B-0071	86%@1.0uM	31.0%@1.0uM		
B-0072	77%@1.0uM	32.0%@1.0uM		
B-0073	91%@1.0uM	24.0%@1.0uM		
B-0074	92%@1.0uM	42.0%@1.0uM		
B-0075	91%@1.0uM	35.0%@1.0uM		
B-0076	58%@1.0uM	21.0%@1.0uM		
B-0077	0.8uM	10.0uM		
B-0078	80%@1.0uM	20.0%@1.0uM		
B-0079	93%@1.0uM	13.0%@1.0uM		
B-0080	73%@1.0uM	73.0%@1.0uM		
B-0081	92%@1.0uM	13.0%@1.0uM		
B-0082	47%@1.0uM	27.0%@1.0uM		
B-0083	0.22uM	6.51uM		
B-0084	56%@1.0uM	30.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0085	83%@1.0uM	21.0%@1.0uM		
B-0086	91%@1.0uM	37.0%@1.0uM		
B-0087	0.55uM	2.26uM	38%@30mpk@-6h	
B-0088	96%@1.0uM	9.0%@1.0uM		
B-0089	0.04uM	3.33uM		
B-0090	98%@1.0uM	52.0%@1.0uM		
B-0091	96%@1.0uM	40.0%@1.0uM		
B-0092	97%@1.0uM	34.0%@1.0uM		
B-0093	3.18 uM	1.25uM	30%@30mpk@-6h	
B-0094	96%@1.0uM	52.0%@1.0uM		
B-0095	98%@1.0uM	38.0%@1.0uM		
B-0096	91%@1.0uM	22.0%@1.0uM		
B-0097	72.0%@10.0uM	38.0%@1.0uM		
B-0098	66.0%@10.0uM	12.0%@1.0uM		
B-0099	43.0% @1.0uM	>1.0uM		
B-0100	75.0% @1.0uM	5.0uM		
B-0101	71.0% @1.0uM	2.11uM		
B-0102	81.0%@1.0uM	15.0%@1.0uM		
B-0103	71.0%@1.0uM	6.0%@1.0uM		
B-0104	56.0% @1.0uM	2.78uM		
B-0105	78.0%@1.0uM	5.0uM		
B-0106	62.0%@1.0uM	5.0uM		
B-0107	0.27uM	5.0uM		
B-0108	61.0%@1.0uM	4.85uM		
B-0109	45.0%@1.0uM	19.0%@1.0uM		
B-0110	66.0%@1.0uM	13.0%@1.0uM		
B-0111	57.0%@1.0uM	>1.0uM		
B-0112	97.0%@1.0uM	1.12uM		
B-0113	75.0%@1.0uM	43.0%@1.0uM		
B-0114	45.0%@1.0uM	3.92uM		
B-0115	47.0%@1.0uM	2.0%@1.0uM		
B-0116	73.0%@1.0uM	35.0%@1.0uM		
B-0117	0.46 uM	1.78 uM	30%@30mpk@-6h	
B-0118	1.18 uM	1.29 uM		
B-0119	89.0%@10.0uM	2.78uM		
B-0120	0.008 uM	0.21 uM	77%@100mpk@-6h	70%@3mpk@-4h
B-0121	79.0%@1.0uM	1.22uM		
B-0122	79.0%@10.0uM	2.0%@1.0uM		
B-0123	59.0%@1.0uM	>1.0uM		
B-0124	73.0%@1.0uM	15.0%@1.0uM		
B-0125	70.0%@10.0uM	17.0%@1.0uM		
B-0126	66.0%@1.0uM	1.57uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0127	82.0% @ 1.0uM	0.96uM		
B-0128	78.0% @ 1.0uM	1.81uM		
B-0129	51.0% @ 1.0uM	31.0% @ 1.0uM		
B-0130	69.0% @ 1.0uM	58.0% @ 1.0uM		
B-0131	43.0% @ 1.0uM	46.0% @ 1.0uM		
B-0132	76.0% @ 1.0uM	8.0% @ 1.0uM		
B-0133	51.0% @ 1.0uM	42.0% @ 1.0uM		
B-0134	60.0% @ 1.0uM	2.17uM		
B-0135	78.0% @ 1.0uM	58.0% @ 1.0uM		
B-0136	77.0% @ 1.0uM	44.0% @ 1.0uM		
B-0137	41.0% @ 1.0uM	37.0% @ 1.0uM		
B-0138	50.0% @ 1.0uM	32.0% @ 1.0uM		
B-0139	54.0% @ 10.0uM	17.0% @ 1.0uM		
B-0140	67% @ 10.0uM	9.0% @ 1.0uM		
B-0141	78.0% @ 1.0uM	10.0% @ 1.0uM		
B-0142	86.0% @ 1.0uM	12.0% @ 1.0uM		
B-0143	42.0% @ 1.0uM	3.63uM		
B-0144	86.0% @ 1.0uM	43.0% @ 1.0uM		
B-0145	54.0% @ 10.0uM	12.0% @ 1.0uM		
B-0146	77.0% @ 10.0uM	28.0% @ 1.0uM		
B-0147	44.0% @ 1.0uM	22.0% @ 1.0uM		
B-0148	51.0% @ 1.0uM	>1.0uM		
B-0149	1.15 uM	10.0 uM		
B-0150	27.0% @ 10.0uM	35.0% @ 1.0uM		
B-0151	43.0% @ 1.0uM	30.0% @ 1.0uM		
B-0152	51.0% @ 1.0uM	24.0% @ 1.0uM		
B-0153	57.0% @ 1.0uM	21.0% @ 1.0uM		
B-0154	65.0% @ 10.0uM	14.0% @ 1.0uM		
B-0155	40.0% @ 10.0uM	26.0% @ 1.0uM		
B-0156	42.0% @ 10.0uM	13.0% @ 1.0uM		
B-0157	48.0% @ 10.0uM	9.0% @ 1.0uM		
B-0158	58.0% @ 10.0uM	39.0% @ 1.0uM		
B-0159	54.0% @ 10.0uM	5.0% @ 1.0uM		
B-0160	59.0% @ 10.0uM	26.0% @ 1.0uM		
B-0161	72.0% @ 10.0uM	13.0% @ 1.0uM		
B-0162	23% @ 1.0uM	2.05 uM		
B-0163	20.0% @ 10.0uM	10.0% @ 1.0uM		
B-0164	37.0% @ 10.0uM	20.0% @ 1.0uM		
B-0165	70.0% @ 10.0uM	19.0% @ 1.0uM		
B-0166	45.0% @ 10.0uM	37.0% @ 1.0uM		
B-0167	40.0% @ 1.0uM	37.0% @ 1.0uM		
B-0168	44% @ 1.0uM	2.36 uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhlib @ dose @predose time	Rat LPS Model % inhlib @dose @predose time
B-0169	43.0% @1.0uM	21.0% @1.0uM		
B-0170	43.0% @1.0uM	30.0% @1.0uM		
B-0171	61.0% @10.0uM	21.0% @1.0uM		
B-0172	16.0% @10.0uM	11.0% @1.0uM		
B-0173	33.0% @10.0uM	48.0% @1.0uM		
B-0174	54.0% @10.0uM	43.0% @1.0uM		
B-0175	41.0% @10.0uM	31.0% @1.0uM		
B-0176	50.0% @1.0uM	30.0% @1.0uM		
B-0177	70.0% @10.0uM	27.0% @1.0uM		
B-0178	12.0% @10.0uM	35.0% @1.0uM		
B-0179	27.0% @10.0uM	37.0% @1.0uM		
B-0180	34.0% @10.0uM	23.0% @1.0uM		
B-0181	5.0% @1.0uM	2.0% @1.0uM		
B-0182	39.0% @10.0uM	40.0% @1.0uM		
B-0183	12.0% @10.0uM	34.0% @1.0uM		
B-0184	66.0% @10.0uM	17.0% @1.0uM		
B-0185	65.0% @10.0uM	25.0% @1.0uM		
B-0186	40.0% @1.0uM	25.0% @1.0uM		
B-0187	4.0% @10.0uM	14.0% @1.0uM		
B-0188	70.0% @10.0uM	35.0% @1.0uM		
B-0189	42.0% @10.0uM	9.0% @1.0uM		
B-0190	59.0% @10.0uM	31.0% @1.0uM		
B-0191	40.0% @1.0uM	29.0% @1.0uM		
B-0192	12.0% @10.0uM	47.0% @1.0uM		
B-0193	0.54 uM	6% @1.0uM		
B-0194	1.31 uM	22% @1.0uM		
B-0195	1.03 uM	55% @1.0uM		
B-0196	2.24 uM	>1.0uM		
B-0197	2.0 uM	14% @1.0uM		
B-0198	1.2 uM	2% @1.0uM		
B-0199	1.34 uM	3% @1.0uM		
B-0200	1.31 uM	16% @1.0uM		
B-0201	0.29 uM	59% @1.0uM		
B-0202	0.55 uM	2.26 uM		
B-0203	0.16 uM	65% @1.0uM		
B-0204	0.21 uM	48% @1.0uM		
B-0205	0.096 uM	54% @1.0uM		
B-0206	5.76 uM	14% @1.0uM		
B-0207	0.12 uM	52% @1.0uM		
B-0208	0.067 uM	>1.0uM		
B-0209	0.29 uM	8% @1.0uM		
B-0210	0.057 uM	67% @1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0211	0.25 uM	30%@1.0uM		
B-0212	0.12 uM	28%@1.0uM		
B-0213	0.31 uM	39%@1.0uM		
B-0214	0.16 uM	50%@1.0uM		
B-0215	0.11 uM	51%@1.0uM		
B-0216	0.56 uM	>1.0uM		
B-0217	0.55 uM	>1.0uM		
B-0218	0.53 uM	18%@1.0uM		
B-0219	0.91 uM	18%@1.0uM		
B-0220	0.13 uM	40%@1.0uM		
B-0221	2.4 uM	>1.0uM		
B-0222	0.4uM	29.0%@1.0uM		
B-0223	0.2uM	1.0%@1.0uM		
B-0224	<0.1uM	93.0%@1.0uM		
B-0225	0.047uM	37.0%@1.0uM		
B-0226	0.074uM	20.0%@1.0uM		
B-0227	0.045uM	1.0%@1.0uM		
B-0228	0.15uM	44.0%@1.0uM		
B-0229	<0.1uM	61.0%@1.0uM		
B-0230	0.041uM	30.0%@1.0uM		
B-0231	0.055uM	40.0%1.0uM		
B-0232	0.048uM	24.0%@1.0uM		
B-0233	0.095uM	43.0%@1.0uM		
B-0234	0.11uM	68.0%@1.0uM		
B-0235	1.31uM	90.0%@1.0uM		
B-0236	0.077uM	46.0%@1.0uM		
B-0237	0.13uM	60.0%@1.0uM		
B-0238	0.47uM	82.0%@1.0uM		
B-0239	5.73uM	84.0%@1.0uM		
B-0240	0.2uM	70.0%@1.0uM		
B-0241	0.1uM	45.0%@1.0uM		
B-0242	<0.1uM	78.0%@1.0uM		
B-0243	0.039uM	53.0%@1.0uM		
B-0244	0.02uM	57.0%@1.0uM		
B-0245	0.13uM	24.0%@1.0uM		
B-0246	<0.1uM	>1.0uM		
B-0247	0.082uM	75.0%@1.0uM		
B-0248	<0.1uM	11.0%@1.0uM		
B-0249	<0.1uM	75.0%@1.0uM		
B-0250	0.28uM	36.0%@1.0uM		
B-0251	0.31uM	1.0%@1.0uM		
B-0252	0.041uM	54.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)



Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0253	0.061uM	74.0%@1.0uM		
B-0254	0.12uM	59.0%@1.0uM		
B-0255	0.32uM	68.0%@1.0uM		
B-0256	<0.1uM	88.0%@1.0uM		
B-0257	1.71uM	11.0%@1.0uM		
B-0258	0.37uM	63.0%@1.0uM		
B-0259	0.35uM	58.0%@1.0uM		
B-0260	0.56uM	23.0%@1.0uM		
B-0261	0.49uM	23.0%@1.0uM		
B-0262	0.41uM	89.0%@1.0uM		
B-0263	0.62uM	64.0%@1.0uM		
B-0264	0.14uM	18.0%@1.0uM		
B-0265	0.92uM	24.0%@1.0uM		
B-0266	0.25uM	24.0%@1.0uM		
B-0267	0.48uM	11.0%@1.0uM		
B-0268	3.39uM	19.0%@1.0uM		
B-0269	9.81uM	19.0%@1.0uM		
B-0270	5.79uM	13.0%@1.0uM		
B-0271	7.55uM	12.0%@1.0uM		
B-0272	1.81uM	48.0%@1.0uM		
B-0273	5.03uM	13.0%@1.0uM		
B-0274	2.68uM	25.0%@1.0uM		
B-0275	2.67uM	33.0%@1.0uM		
B-0276	1.25uM	26.0%@1.0uM		
B-0277	0.68uM	34.0%@1.0uM		
B-0278	1.26uM	36.0%@1.0uM		
B-0279	1.39uM	33.0%@1.0uM		
B-0280	0.86uM	18.0%@1.0uM		
B-0281	7.37uM	24.0%@1.0uM		
B-0282	0.75uM	38.0%@1.0uM		
B-0283	6.66uM	29.0%@1.0uM		
B-0284	0.083uM	65.0%@1.0uM		
B-0285	4.57uM	29.0%@1.0uM		
B-0286	0.33uM	50.0%@1.0uM		
B-0287	4.0uM	22.0%@1.0uM		
B-0288	4.46uM	26.0%@1.0uM		
B-0289	0.15uM	55.0%@1.0uM		
B-0290	0.66uM	44.0%@1.0uM		
B-0291	1.33uM	20.0%@1.0uM		
B-0292	0.22uM	28.0%@1.0uM		
B-0293	0.66uM	53.0%@1.0uM		
B-0294	0.68uM	45.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0295	0.82uM	45.0%@1.0uM		
B-0296	8.03uM	36.0%@1.0uM		
B-0297	0.78uM	30.0%@1.0uM		
B-0298	0.58uM	48.0%@1.0uM		
B-0299	0.87uM	54.0%@1.0uM		
B-0300	0.78uM	32.0%@1.0uM		
B-0301	0.19uM	50.0%@1.0uM		
B-0302	4.02uM	24.0%@1.0uM		
B-0303	0.22uM	10.0%@1.0uM		
B-0304	0.56uM	28.0%@1.0uM		
B-0305				
B-0306				
B-0307				
B-0308				
B-0309				
B-0310				
B-0311				
B-0312				
B-0313				
B-0314				
B-0315				
B-0316				
B-0317				
B-0318				
B-0319				
B-0320				
B-0321				
B-0322				
B-0323				
B-0324				
B-0325				
B-0326				
B-0327				
B-0328				
B-0329				
B-0330				
B-0331				
B-0332				
B-0333				
B-0334				
B-0335				
B-0336				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0337				
B-0338				
B-0339				
B-0340				
B-0341				
B-0342				
B-0343				
B-0344				
B-0345				
B-0346				
B-0347				
B-0348				
B-0349				
B-0350				
B-0351				
B-0352				
B-0353	1.37uM	55%@1.0uM		
B-0354	1.0uM	0.66uM	51%@30mpk@-6h	54%@3mpk@-4h
B-0355	0.75uM	40.0%@1.0uM		
B-0356	0.66uM	24.0%@1.0uM		
B-0357	1.46uM	0.66uM		
B-0358	0.37uM	17.0%@1.0uM		
B-0359	0.45uM	47.0%@1.0uM		
B-0360	1.6uM	19.0%@1.0uM		
B-0361	0.33uM	46.0%@1.0uM		
B-0362	0.52uM	27.0%@1.0uM		
B-0363	4.67uM	25.0%@1.0uM		
B-0364	1.44uM	27.0%@1.0uM		
B-0365	0.96uM	27.0%@1.0uM		
B-0366	0.7uM	46.0%@1.0uM		
B-0367	1.0uM	23.0%@1.0uM		
B-0368	1.0uM	0.64uM	37%@30mpk@-6h	
B-0369	0.16uM	57.0%@1.0uM		
B-0370	0.65uM	28.0%@1.0uM		
B-0371	0.49uM	28.0%@1.0uM		
B-0372	0.35uM	29.0%@1.0uM		
B-0373	0.45uM	18.0%@1.0uM		
B-0374	1.38uM	12.0%@1.0uM		
B-0375	1.0uM	19.0%@1.0uM		
B-0376	2.99uM	12.0%@1.0uM		
B-0377	1.29uM	36.0%@1.0uM		
B-0378	1.1uM	36.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0379	0.53uM	24.0%@1.0uM		
B-0380	1.41uM	32.0%@1.0uM		
B-0381	0.22uM	47.0%@1.0uM		
B-0382	0.41uM	32.0%@1.0uM		
B-0383	1.43uM	10.0%@1.0uM		
B-0384	4.02uM	16.0%@1.0uM		
B-0385	0.057uM	0.9uM	30%@30mpk@-6h	0%@3mpk@-4h
B-0386	0.13uM	54.0%@1.0uM		
B-0387	0.41uM	52.0%@1.0uM		
B-0388	<0.1uM	36.0%@1.0uM		
B-0389	0.01uM	0.05uM		62%@3mpk@-4h
B-0390	0.089uM	55.0%@1.0uM		
B-0391	0.86uM	18.0%@1.0uM		
B-0392	0.13uM	57.0%@1.0uM		
B-0393	0.043uM	66.0%@1.0uM		
B-0394	0.13uM	45.0%@1.0uM		
B-0395	0.087uM	48.0%@1.0uM		
B-0396	0.097uM	0.44uM		
B-0397	0.17uM	41.0%@1.0uM		
B-0398	0.054uM	66.0%@1.0uM		
B-0399	0.14uM	39.0%@1.0uM		
B-0400	0.16uM	25.0%@1.0uM		
B-0401	0.46uM	52.0%@1.0uM		
B-0402	0.14uM	1.51uM		
B-0403	1.77uM	2.42uM		
B-0404	0.31uM	48.0%@1.0uM		
B-0405	0.79uM	30.0%@1.0uM		
B-0406	0.54uM	35.0%@1.0uM		
B-0407	0.76uM	27.0%@1.0uM		
B-0408	0.5uM	50.0%@1.0uM		
B-0409	0.53uM	30.0%@1.0uM		
B-0410	0.38uM	44.0%@1.0uM		
B-0411	0.62uM	50.0%@1.0uM		
B-0412	0.24uM	48.0%@1.0uM		
B-0413	0.18uM	55.0%@1.0uM		
B-0414	2.54uM	25.0%@1.0uM		
B-0415	0.42uM	43.0%@1.0uM		
B-0416	0.32uM	34.0%@1.0uM		
B-0417	0.91uM	28.0%@1.0uM		
B-0418	0.22uM	27.0%@1.0uM		
B-0419	0.85uM	41.0%21.0uM		
B-0420	0.83uM	49.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhlib @ dose @predose time	Rat LPS Model % inhlib @dose @predose time
B-0421	0.46uM	57.0%@1.0uM		
B-0422	<0.1uM	40.0%@1.0uM		
B-0423	0.18uM	33.0%@1.0uM		
B-0424	0.083uM	32.0%@1.0uM		
B-0425	0.26uM	54.0%@1.0uM		
B-0426	0.055uM	0.74uM		41%@3mpk@-4h
B-0427	0.63uM	39.0%@1.0uM		
B-0428	0.99uM	27.0%@1.0uM		
B-0429	0.27uM	45.0%@1.0uM		
B-0430	0.29uM	75.0%@1.0uM		
B-0431	0.21uM	64.0%@1.0uM		
B-0432	<0.1uM	89.0%@1.0uM		
B-0433	<0.1uM	92.0%@1.0uM		
B-0434	0.12uM	65.0%@1.0uM		
B-0435	0.3uM	61.0%@1.0uM		
B-0436	1.11uM	71.0%@1.0uM		
B-0437	0.58uM	59.0%@1.0uM		
B-0438	<0.1uM	91.0%@1.0uM		
B-0439	2.12uM	65.0%@1.0uM		
B-0440	0.66uM	63.0%@1.0uM		
B-0441	0.8uM	58.0%@1.0uM		
B-0442	<0.1uM	91.0%@1.0uM		
B-0443	2.01uM	71.0%@1.0uM		
B-0444	1.01uM	51.0%@1.0uM		
B-0445	<0.1uM	83.0%@1.0uM		
B-0446	0.78uM	80.0%@1.0uM		
B-0447	0.19uM	71.0%@1.0uM		
B-0448	0.4uM	79.0%@1.0uM		
B-0449	0.83uM	81.0%@1.0uM		
B-0450	0.26uM	81.0%@1.0uM		
B-0451	0.071uM	83.0%@1.0uM	42%@30mpk@-6h	
B-0452	0.7uM	75.0%@1.0uM		
B-0453	0.47uM	75.0%@1.0uM		
B-0454	0.11uM	80.0%@1.0uM		
B-0455	<0.1uM	95.0%@1.0uM		36%@3mpk%-4h
B-0456	1.81uM	67.0%@1.0uM		
B-0457	0.089uM	81.0%@1.0uM		
B-0458	0.033uM	70.0%@1.0uM		
B-0459	0.099uM	76.0%@1.0uM		
B-0460	0.061uM	92.0%@1.0uM		
B-0461	0.025uM	96.0%@1.0uM		
B-0462	<0.1uM	97.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0463	0.052uM	95.0%@1.0uM		
B-0464	<0.1uM	91.0%@1.0uM		
B-0465	0.084uM	98.0%@1.0uM		
B-0466	<0.1uM	98.0%@1.0uM		0%@3mpk@-4h
B-0467	<0.1uM	77.0%@1.0uM		
B-0468	0.031uM	93.0%@1.0uM		
B-0469	0.056uM	92.0%@1.0uM		
B-0470	0.063uM	92.0%@1.0uM		
B-0471	0.027uM	97.0%@1.0uM		
B-0472	0.19uM	54.0%@1.0uM		
B-0473	0.004uM	95.0%@1.0uM		
B-0474	0.024uM	86.0%@1.0uM		
B-0475	0.21uM	74.0%@1.0uM		
B-0476	0.56uM	69.0%@1.0uM		
B-0477	1.48uM	96.0%@1.0uM		
B-0478	0.034uM	87.0%@1.0uM		
B-0479	0.031uM	90.0%@1.0uM		15%@3mpk@-4h
B-0480	0.12uM	88.0%@1.0uM		
B-0481	0.014uM	95.0%@1.0uM		56%@3mpk@-4h
B-0482	0.97uM	68.0%@1.0uM		
B-0483	0.57uM	68.0%@1.0uM		
B-0484	0.28uM	62.0%@1.0uM		
B-0485	0.04uM	95.0%@1.0uM		
B-0486	0.24uM	80.0%@1.0uM		
B-0487	0.11uM	89.0%@1.0uM		54%@3mpk@-4h
B-0488	0.62uM	88.0%@1.0uM		
B-0489	0.3uM	80.0%@1.0uM		
B-0490	0.91uM	74.0%@1.0uM		
B-0491	0.43uM	66.0%@1.0uM		
B-0492	0.069uM	42.0%@1.0uM		
B-0493	0.3uM	36.0%@1.0uM		
B-0494	0.13uM	30.0%@1.0uM		
B-0495	0.12uM	25.0%@1.0uM		
B-0496	0.83uM	16.0%@1.0uM		
B-0497	0.44uM	31.0%@1.0uM		
B-0498	0.33uM	11.0%@1.0uM		
B-0499	0.39uM	37.0%@1.0uM		
B-0500	0.26uM	41.0%@1.0uM		
B-0501	0.049uM	52.0%@1.0uM		
B-0502	0.065uM	48.0%@1.0uM		
B-0503	0.16uM	73.0%@1.0uM		
B-0504	0.4uM	43.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0505	0.28uM	44.0%@1.0uM		
B-0506	0.94uM	43.0%@1.0uM		
B-0507	0.18uM	75.0%@1.0uM		
B-0508	2.0uM	48.0%@1.0uM		
B-0509	0.1uM	86.0%@1.0uM		
B-0510	0.69uM	61.0%@1.0uM		
B-0511	0.007uM	90.0%@1.0uM		
B-0512	1.0uM	53.0%@1.0uM		
B-0513	0.72uM	52.0%@1.0uM		
B-0514	0.14uM	87.0%@1.0uM		
B-0515	0.42uM	61.0%@1.0uM		
B-0516	0.37uM	84.0%@1.0uM		
B-0517	0.094uM	52.0%@1.0uM		
B-0518	0.11uM	64.0%@1.0uM		
B-0519	0.043uM	87.0%@1.0uM		
B-0520	0.4uM	67.0%@1.0uM		
B-0521	1.37uM	52.0%@1.0uM		
B-0522	0.15uM	75.0%@1.0uM		
B-0523	0.19uM	83.0%@1.0uM		
B-0524	0.4uM	77.0%@1.0uM		
B-0525	0.16uM	76.0%@1.0uM		
B-0526	0.031uM	87.0%@1.0uM		
B-0527	1.09uM	63.0%@1.0uM		
B-0528	0.14uM	70.0%@1.0uM		
B-0529	0.11uM	73.0%@1.0uM		
B-0530	5.53uM	45.0%@1.0uM		
B-0531	0.5uM	48.0%@1.0uM		
B-0532	0.45uM	1.01uM	41%@30mpk@-6h	
B-0533	1.23uM	47.0%@1.0uM		
B-0534	0.41uM	54.0%@1.0uM		
B-0535	0.44uM	0.87uM		
B-0536	0.46uM	0.15uM		
B-0537	3.44uM	51.0%@1.0uM		
B-0538	1.13uM	45.0%@1.0uM		
B-0539	2.84uM	21.0%@1.0uM		
B-0540	3.62uM	54.0%@1.0uM		
B-0541	3.24uM	28.0%@1.0uM		
B-0542	1.55uM	50.0%@1.0uM		
B-0543	1.56uM	43.0%@1.0uM		
B-0544	1.12uM	27.0%@1.0uM		
B-0545	1.06uM	41.0%@1.0uM		
B-0546	1.04uM	18.0%@1.0uM		
B-0547	1.24uM	21.0%@1.0uM		
B-0548	1.77uM	28.0%@1.0uM		
B-0549	2.22uM	22.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0550	2.41uM	14.0%@1.0uM		
B-0551	1.08uM	56.0%@1.0uM		
B-0552	0.13uM	46.0%@1.0uM		
B-0553	1.44uM	47.0%@1.0uM		
B-0554	2.58uM	20.0%@1.0uM		
B-0555	1.87uM	34.0%@1.0uM		
B-0556	0.49uM	39.0%@1.0uM		
B-0557	1.37uM	32.0%@1.0uM		
B-0558	0.85uM	33.0%@1.0uM		
B-0559	0.53uM	49.0%@1.0uM		
B-0560	2.57uM	31.0%@1.0uM		
B-0561	2.07uM	40.0%@1.0uM		
B-0562	0.22uM	0.3uM		5%@3mpk@-4h
B-0563	0.18uM	0.13uM		
B-0564	0.82uM	58%@1.0uM		
B-0565	0.23uM	0.59uM		
B-0566	<0.1uM	0.17uM		0%@3mpk@-4h
B-0567	0.14uM	0.28uM		
B-0568	1.22uM	46.0%@1.0uM		
B-0569	0.15uM	0.26uM		
B-0570	0.27uM	46.0%@1.0uM		
B-0571	0.38uM	44.0%@1.0uM		
B-0572	0.27uM	41.0%@1.0uM		
B-0573	0.36uM	1.7uM		
B-0574	0.13uM	0.66uM		37%@3mpk@-4h
B-0575	0.032uM	0.17uM		
B-0576	0.068uM	0.39uM		65%@3mpk@-4h
B-0577	0.091uM	66.0%@1.0uM		
B-0578	1.88uM	47.0%@1.0uM		
B-0579	0.11uM	79.0%@1.0uM		
B-0580	2.23uM	0.84uM		
B-0581	0.26uM	2.17uM		
B-0582	1.03uM	37.0%@1.0uM		
B-0583	3.93uM	26.0%@1.0uM		
B-0584	0.66uM	54.0%@1.0uM		
B-0585	0.83uM	79.0%@1.0uM	50%@30mpk@-6h	
B-0586	0.81uM	51.0%@1.0uM		
B-0587	6.84uM	38%@1.0uM		
B-0588	12.8uM	42%@1.0uM		
B-0589	1.71uM	42%@1.0uM		
B-0590	1.57uM	38.0uM		
B-0591	3.59uM	29.0%@1.0uM		
B-0592	1.62uM	45.0%@1.0uM		
B-0593	1.22uM	36.0%@1.0uM		
B-0594	-	41.0%@1.0uM		
B-0595	2.42uM	22.0%@1.0uM		
B-0596	20.0uM	41.0%@1.0uM		
B-0597	1.68uM	63.0%@1.0uM		
B-0598	2.12uM	50.0%@1.0uM		



Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0599	4.16uM	21.0%@1.0uM		
B-0600	0.002uM	28.0%@1.0uM		
B-0601	0.089uM	1.31uM		43%@3mpk%-4h
B-0602	0.97uM	61.0%@1.0uM		
B-0603	0.09uM	51.0%@1.0uM		
B-0604	0.3uM	20.0%@1.0uM		
B-0605	0.18uM	47.0%@1.0uM		
B-0606	0.17uM	53.0%@1.0uM		
B-0607	2.79uM	70.0%@1.0uM		
B-0608	0.059uM	73.0%@1.0uM		
B-0609	<0.1uM	87.0%@1.0uM		
B-0610	<0.1uM	88.0%@1.0uM		
B-0611	0.65uM	60.0%@1.0uM		
B-0612	0.16uM	60.0%@1.0uM		
B-0613	0.17uM	76.0%@1.0uM		
B-0614	0.76uM	70.0%@1.0uM		0%@3mpk@-4h
B-0615	0.08uM	83.0%@1.0uM		
B-0616	0.38uM	87.0%@1.0uM		
B-0617	0.045uM	92.0%@1.0uM		
B-0618	0.37uM	80.0%@1.0uM		
B-0619	<0.1uM	88.0%@1.0uM		
B-0620	1.59uM	58.0%@1.0uM		
B-0621	0.36uM	68.0%@1.0uM		
B-0622	0.076uM	78.0%@1.0uM		
B-0623	0.12uM	76.0%@1.0uM		
B-0624	0.085uM	54.0%@1.0uM		
B-0625	0.023uM	88.0%@1.0uM		
B-0626	<0.1uM	85.0%@1.0uM		
B-0627	0.25uM	69.0%@1.0uM		
B-0628	0.023uM	72.0%@1.0uM		
B-0629	0.2uM	79.0%@1.0uM		
B-0630	0.06uM	77.0%@1.0uM		
B-0631	0.065uM	81.0%@1.0uM		
B-0632	<0.1uM	79.0%@1.0uM		
B-0633	0.6uM	80.0%@1.0uM		
B-0634	0.6uM	40.0%@1.0uM		
B-0635	0.15uM	55.0%@1.0uM		
B-0636	<0.1uM	86.0%@1.0uM		
B-0637	0.11uM	92.0%@1.0uM		
B-0638	0.25uM	89.0%@1.0uM		
B-0639	0.051uM	93.0%@1.0uM		50%@3mpk@-4h
B-0640	0.36uM	94.0%@1.0uM		
B-0641	0.58uM	65.0%@1.0uM		
B-0642	0.49uM	90.0%@1.0uM		
B-0643	0.069uM	85.0%@1.0uM		0%@3mpk@-4h
B-0644	0.058uM	89.0%@1.0uM		
B-0645	0.58uM	80.0%@1.0uM		
B-0646	0.26uM	94.0%@1.0uM		
B-0647	1.61uM	76.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0648	<0.1uM	83.0% @ 1.0uM		
B-0649	0.83uM	39.0% @ 1.0uM		
B-0650	0.006uM	95.0% @ 1.0uM		8% @ 3mpk @ -4h
B-0651	1.78uM	81.0% @ 1.0uM		
B-0652	0.19uM	83.0% @ 1.0uM		
B-0653	2.01uM	74.0% @ 1.0uM		
B-0654	5.97uM	78.0% @ 1.0uM		
B-0655	1.25uM	76.0% @ 1.0uM		
B-0656	0.007uM	95.0% @ 1.0uM		28% @ 3mpk @ -4h
B-0657	0.17uM	83.0% @ 1.0uM		
B-0658	1.14uM	91.0% @ 1.0uM		
B-0659	2.64uM	87.0% @ 1.0uM		
B-0660	0.088uM	92.0% @ 1.0uM		
B-0661	<0.1uM	90.0% @ 1.0uM		
B-0662	<0.1uM	95.0% @ 1.0uM		
B-0663	0.88uM	74.0% @ 1.0uM		
B-0664	0.39uM	80.0% @ 1.0uM		
B-0665	0.47uM	72.0% @ 1.0uM		
B-0666	0.17uM	73.0% @ 1.0uM		
B-0667	0.83uM	75.0% @ 1.0uM		
B-0668	0.27uM	78.0% @ 1.0uM		
B-0669	0.89uM	34.0% @ 1.0uM		
B-0670	3.15uM	32.0% @ 1.0uM		
B-0671	6.38uM	36.0% @ 1.0uM		
B-0672	6.59uM	32.0% @ 1.0uM		
B-0673	8.54uM	48.0% @ 1.0uM		
B-0674	2.81uM	42.0% @ 1.0uM		
B-0675	5.42uM	3.0% @ 1.0uM		
B-0676	2.09uM	22.0% @ 1.0uM		
B-0677	1.63uM	25.0% @ 1.0uM		
B-0678	0.38uM	52.0% @ 1.0uM		
B-0679	0.062uM	45.0% @ 1.0uM		
B-0680	0.42uM	67.0% @ 1.0uM		
B-0681	1.96uM	17.0% @ 1.0uM		
B-0682	0.76uM	39.0% @ 1.0uM		
B-0683	13.0uM	32.0% @ 1.0uM		
B-0684	0.54uM	68.0% @ 1.0uM		
B-0685	15.4uM	33.0% @ 1.0uM		
B-0686	0.42uM	59.0% @ 1.0uM		
B-0687	10.1uM	15.0% @ 1.0uM		
B-0688	0.66uM	58.0% @ 1.0uM		
B-0689	14.6uM	27.0% @ 1.0uM		
B-0690	27.1uM	36.0% @ 1.0uM		
B-0691	0.16uM	48.0% @ 1.0uM		
B-0692	0.38uM	29.0% @ 1.0uM		
B-0693	0.39uM	28.0% @ 1.0uM		
B-0694	0.62uM	21.0% @ 1.0uM		
B-0695	0.23uM	32.0% @ 1.0uM		
B-0696	0.085uM	35.0% @ 1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0697	0.45uM	44.0%@1.0uM		
B-0698	2.33uM	43.0%@1.0uM		
B-0699	0.34uM	31.0%@1.0uM		
B-0700	0.24uM	56.0%@1.0uM		
B-0701	0.39uM	45.0%@1.0uM		
B-0702	0.036uM	39.0%@1.0uM		
B-0703	0.12uM	39.0%@1.0uM		
B-0704	2.19uM	29.0%@1.0uM		
B-0705	0.44uM	21.0%@1.0uM		
B-0706	0.44uM	32.0%@1.0uM		
B-0707	1.7uM			
B-0708	2.1uM			
B-0709	0.84uM			
B-0710	1.99uM			
B-0711	1.99uM			
B-0712	2.9uM			
B-0713	4.3uM			
B-0714	3.7uM			
B-0715	3.2uM			
B-0716	4.6uM			
B-0717	4.3uM			
B-0718	1.4uM			
B-0719	3.4uM			
B-0720	1.3uM			
B-0721	3.8uM			
B-0722	0.07uM	>1.0uM		
B-0723	0.47uM			
B-0724	0.06uM	17.0%@1.0uM		
B-0725	9.7uM			
B-0726	1.4uM			
B-0727	0.51uM			
B-0728	20.0uM			
B-0729	0.87uM			
B-0730	0.25uM	11.0%@1.0uM		
B-0731	0.87uM	>1.0uM		
B-0732	14.0uM			
B-0733	32.0uM			
B-0734	0.92uM			
B-0735	1.0uM			
B-0736	26.0uM			
B-0737	2.6uM			
B-0738	2.7uM			
B-0739	4.1uM			
B-0740	4.4uM			
B-0741	26.0uM			
B-0742	2.2uM			
B-0743	1.2uM			
B-0744	23.0uM			
B-0745	6.0uM			

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0746	0.01uM	22.0%@1.0uM		
B-0747	1.1uM			
B-0748	1.2uM			
B-0749	4.4uM			
B-0750	0.92uM			
B-0751	1.6uM			
B-0752	0.33uM			
B-0753	0.37uM			
B-0754	0.55uM			
B-0755	2.3uM			
B-0756	0.94uM			
B-0757	0.54uM	16.0%@1.0uM		
B-0758	1.5uM			
B-0759	0.3uM			
B-0760	0.01uM	13.0%@1.0uM		
B-0761	<0.1uM			
B-0762	0.13uM	5.0%@1.0uM		
B-0763	0.015uM	17.0%@1.0uM		
B-0764	0.67uM	26.0%@1.0uM		
B-0765	0.3uM	29.0%@1.0uM		
B-0766	0.95uM			
B-0767	0.08uM			
B-0768	1.4uM			
B-0769	12.7uM			
B-0770	2.3uM			
B-0771	0.5uM			
B-0772	0.8uM			
B-0773	14.0uM			
B-0774	1.5uM			
B-0775	0.6uM	>1.0uM		
B-0776	0.9uM	>1.0uM		
B-0777	21.0uM			
B-0778	51.0uM			
B-0779	0.5uM			
B-0780	1.1uM			
B-0781	48.0uM			
B-0782	22.0uM			
B-0783	8.0uM			
B-0784	7.0uM			
B-0785	23.0uM			
B-0786	24.0uM			
B-0787	1.5uM			
B-0788	1.2uM			
B-0789	33.0uM			
B-0790	1.0uM	4.0%@1.0uM		
B-0791	0.3uM	>1.0uM		
B-0792	1.1uM			
B-0793	0.3uM			
B-0794	2.9uM	2.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM-or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0795	1.9uM	11.0%@1.0uM		
B-0796	1.4uM			
B-0797	1.04uM	-		
B-0798	1.73uM	-		
B-0799	-	>1.0uM		
B-0800	1.01uM	>1.0uM		
B-0801	0.67uM	>1.0uM		
B-0802	-	>1.0uM		
B-0803	0.057uM	53.0%@1.0uM		
B-0804	0.3uM	32.0%@1.0uM		
B-0805	0.71uM	>1.0uM		
B-0806	3.28uM	>1.0uM		
B-0807	10.8uM	-		
B-0808	3.09uM	>1.0uM		
B-0809	1.22uM	7.0%@1.0uM		
B-0810	1.11uM	>1.0uM		
B-0811	2.79uM	2.0%@1.0uM		
B-0812	2.12uM	>1.0uM		
B-0813	3.02uM	>1.0uM		
B-0814	-	>1.0uM		
B-0815	2.11uM	>1.0uM		
B-0816	3.46uM	>1.0uM		
B-0817	3.07uM	33.0%@1.0uM		
B-0818	4.97uM	>1.0uM		
B-0819	1.08uM	>1.0uM		
B-0820	1.64uM	3.0%@1.0uM		
B-0821	1.44uM	-		
B-0822	1.33uM	-		
B-0823	2.39uM	>1.0uM		
B-0824	3.41uM	-		
B-0825	-	-		
B-0826	1.74uM	-		
B-0827	15.6uM	-		
B-0828	7.9uM	-		
B-0829	0.61uM	65.0%@1.0uM		
B-0830	0.54uM	34.0%@1.0uM		
B-0831	0.9uM	>1.0uM		
B-0832	1.49uM	-		
B-0833	0.95uM	23.0%@1.0uM		
B-0834	1.25uM	-		
B-0835	-	-		
B-0836	1.24uM	-		
B-0837	1.96uM	>1.0uM		
B-0838	3.1uM	-		
B-0839	4.3uM	-		
B-0840	0.63uM	47.0%@1.0uM		
B-0841	0.32uM	36.0%@1.0uM		
B-0842	0.74uM	63.0%@1.0uM		
B-0843	0.61uM	>1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0844	0.4uM	25.0%@1.0uM		
B-0845	1.78uM	-		
B-0846	1.8uM	-		
B-0847	0.73uM	21.0%@1.0uM		
B-0848	1.56uM	-		
B-0849	1.25uM	-		
B-0850	1.81uM	-		
B-0851	0.91uM	39.0%@1.0uM		
B-0852	1.02uM	-		
B-0853	-	38.0%@1.0uM		
B-0854	-	25.0%@1.0uM		
B-0855	-	8.0%@1.0uM		
B-0856	-	38.0%@1.0uM		
B-0857	6.25uM	-		
B-0858	2.1uM	48.0%@1.0uM		
B-0859	39.5uM	-		
B-0860	38.1uM	-		
B-0861	1.32uM	12.0%@1.0uM		
B-0862	2.15uM	4.0%@1.0uM		
B-0863	0.81uM	25.0%@1.0uM		
B-0864	0.39uM	40.0%@1.0uM		
B-0865	0.66uM	46.0%@1.0uM		
B-0866	1.38uM	28.0%@1.0uM		
B-0867	0.62uM	>1.0uM		
B-0868	3.28uM	8.0%@1.0uM		
B-0869	4.19uM	>1.0uM		
B-0870	3.13uM	>1.0uM		
B-0871	1.9uM	>1.0uM		
B-0872	3.13uM	3.0%@1.0uM		
B-0873	6.92uM	>1.0uM		
B-0874	1.92uM	>1.0uM		
B-0875	2.13uM	8%@1.0uM		
B-0876	0.89uM	>1.0uM		
B-0877	1.17uM	13.0%@1.0uM		
B-0878	0.65uM	19.0%@1.0uM		
B-0879	0.87uM	1.0%@1.0uM		
B-0880	0.15uM	40.0%@1.0uM		
B-0881	1.36uM	>1.0uM		
B-0882	1.48uM	9%@1.0uM		
B-0883	1.06uM	>1.0uM		
B-0884	1.89uM	-		
B-0885				
B-0886				
B-0887				
B-0888				
B-0889				
B-0890				
B-0891				
B-0892				

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0893				
B-0894				
B-0895				
B-0896				
B-0897				
B-0898				
B-0899				
B-0900				
B-0901				
B-0902				
B-0903				
B-0904				
B-0905				
B-0906				
B-0907				
B-0908				
B-0909				
B-0910				
B-0911				
B-0912				
B-0913				
B-0914				
B-0915				
B-0916				
B-0917				
B-0918				
B-0919				
B-0920				
B-0921				
B-0922				
B-0923				
B-0924				
B-0925				
B-0926				
B-0927				
B-0928				
B-0929				
B-0930				
B-0931				
B-0932				
B-0933	47.0%@1.0uM	37.0%@1.0uM		
B-0934	67.0%@1.0uM	36.0%@1.0uM		
B-0935	69.0%@1.0uM	54.0%@1.0uM		
B-0936	69.0%@1.0uM	>1.0uM		
B-0937	64.0%@1.0uM	1.74uM		
B-0938	51.0%@1.0uM	29.0%@1.0uM		
B-0939	78.0%@1.0uM	14.0%@1.0uM		
B-0940	56.0%@1.0uM	22.0%@1.0uM		
B-0941	81.0%@1.0uM	25.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0942	82.0% @ 1.0uM	2.0% @ 1.0uM		
B-0943	63.0% @ 10.0uM	24.0% @ 1.0uM		
B-0944	45.0% @ 1.0uM	27.0% @ 1.0uM		
B-0945	96.0% @ 1.0uM	0.93uM		
B-0946	76.0% @ 1.0uM	31.0% @ 1.0uM		
B-0947	69.0% @ 1.0uM	34.0% @ 1.0uM		
B-0948	68.0% @ 1.0uM	1.81uM		
B-0949	90.0% @ 1.0uM	17.0% @ 1.0uM		
B-0950	81.0% @ 1.0uM	0.58uM		
B-0951	82.0% @ 1.0uM	20.0% @ 1.0uM		
B-0952	44.0% @ 1.0uM	21.0% @ 1.0uM		
B-0953	63.0% @ 1.0uM	25.0% @ 1.0uM		
B-0954	62.0% @ 1.0uM	0.52uM		
B-0955	49.0% @ 1.0uM	0.54uM		
B-0956	56.0% @ 1.0uM	1.33uM		
B-0957	79.0% @ 1.0uM	22.0% @ 1.0uM		
B-0958	74.0% @ 1.0uM	0.38uM		
B-0959	83.0% @ 1.0uM	39.0% @ 1.0uM		
B-0960	48.0% @ 1.0uM	4.0% @ 1.0uM		
B-0961	79.0% @ 1.0uM	23.0% @ 1.0uM		
B-0962	85.0% @ 1.0uM	2.71uM		
B-0963	76.0% @ 1.0uM	39.0% @ 1.0uM		
B-0964	94.0% @ 1.0uM	5.0uM		
B-0965	74.0% @ 1.0uM	1.1uM		
B-0966	50.0% @ 1.0uM	5.0% @ 1.0uM		
B-0967	80.0% @ 1.0uM	29.0% @ 1.0uM		
B-0968	35.0% @ 1.0uM	26.0% @ 1.0uM		
B-0969	63.0% @ 1.0uM	35.0% @ 1.0uM		
B-0970	76.0% @ 10.0uM	0.88uM		
B-0971	61.0% @ 1.0uM	39.0% @ 1.0uM		
B-0972	85.0% @ 1.0uM	2.0% @ 1.0uM		
B-0973	66.0% @ 10.0uM	48.0% @ 1.0uM		
B-0974	57.0% @ 1.0uM	47.0% @ 1.0uM		
B-0975	82.0% @ 1.0uM	32.0% @ 1.0uM		
B-0976	79.0% @ 1.0uM	36.0% @ 1.0uM		
B-0977	60.0% @ 1.0uM	26.0% @ 1.0uM		
B-0978	59.0% @ 1.0uM	36.0% @ 1.0uM		
B-0979	56.0% @ 10.0uM	23.0% @ 1.0uM		
B-0980	68.0% @ 1.0uM	31.0% @ 1.0uM		
B-0981	62.0% @ 1.0uM	57.0% @ 1.0uM		
B-0982	65.0% @ 1.0uM	23.0% @ 1.0uM		
B-0983	75.0% @ 1.0uM	0.8uM		
B-0984	60.0% @ 1.0uM	51.0% @ 1.0uM		
B-0985	86.0% @ 1.0uM	0.75uM		
B-0986	70.0% @ 1.0uM	71.0% @ 1.0uM		
B-0987	78.0% @ 1.0uM	79.0% @ 1.0uM		
B-0988	72.0% @ 1.0uM	65.0% @ 1.0uM		
B-0989	85.0% @ 1.0uM	0.85uM		
B-0990	-	26.0% @ 1.0uM		

SUBSTITUTE SHEET (RULE 26)



Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0991	58.0%@1.0uM	33.0%@1.0uM		
B-0992	77.0%@1.0uM	45.0%@1.0uM		
B-0993	57.0%@1.0uM	73.0%@1.0uM		
B-0994	55.0%@1.0uM	43.0%@1.0uM		
B-0995	53.0%@1.0uM	14.0%@1.0uM		
B-0996	54.0%@1.0uM	27.0%@1.0uM		
B-0997	69.0%@1.0uM	22.0%@1.0uM		
B-0998	67.0%@1.0uM	25.0%@1.0uM		
B-0999	61.0%@1.0uM	24.0%@1.0uM		
B-1000	55.0%@1.0uM	42.0%@1.0uM		
B-1001	63.0%@1.0uM	31.0%@1.0uM		
B-1002	70.0%@1.0uM	41.0%@1.0uM		
B-1003	74.0%@1.0uM	29.0%@1.0uM		
B-1004	79.0%@1.0uM	45.0%@1.0uM		
B-1005	58.0%@1.0uM	23.0%@1.0uM		
B-1006	69.0%@1.0uM	38.0%@1.0uM		
B-1007	52.0%@1.0uM	34.0%@1.0uM		
B-1008	54.0%@1.0uM	23.0%@1.0uM		
B-1009	80.0%@1.0uM	55.0%@1.0uM		
B-1010	75.0%@1.0uM	1.0uM		
B-1011	72.0%21.0uM	17.0%@1.0uM		
B-1012	-	20.0%@1.0uM		
B-1013	85.0%@1.0uM	7.0%@1.0uM		
B-1014	88.0%@1.0uM	20.0%@1.0uM		
B-1015	77.0%@1.0uM	34.0%@1.0uM		
B-1016	58.0%@1.0uM	10.0%@1.0uM		
B-1017	96.0%@1.0uM	58.0%@1.0uM		
B-1018	88.0%@1.0uM	34.0%@1.0uM		
B-1019	82.0%@1.0uM	66.0%@1.0uM		
B-1020	87.0%@1.0uM	36.0%@1.0uM		
B-1021	82.0%@1.0uM	35.0%@1.0uM		
B-1022	84.0%@1.0uM	53.0%@1.0uM		
B-1023	93.0%@1.0uM	70.0%@1.0uM		
B-1024	89.0%@1.0uM	57.0%@1.0uM		
B-1025	61.0%@1.0uM	23.0%@1.0uM		
B-1026	87.0%@1.0uM	53.0%@1.0uM		
B-1027	58.0%@1.0uM	18.0%@1.0uM		
B-1028	70.0%@1.0uM	17.0%@1.0uM		
B-1029	69.0%@1.0uM	54.0%@1.0uM		
B-1030	76.0%@1.0uM	60.0%@1.0uM		
B-1031	69.0%@1.0uM	42.0%@1.0uM		
B-1032	76.0%@1.0uM	37.0%@1.0uM		
B-1033	86.0%@1.0uM	34.0%@1.0uM		
B-1034	66.0%@1.0uM	39.0%@1.0uM		
B-1035	75.0%@1.0uM	52.0%@1.0uM		
B-1036	68.0%@1.0uM	68.0%@1.0uM		
B-1037	-	41.0%@1.0uM		
B-1038	57.0%@1.0uM	0.57uM		
B-1039	-	1.33uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1040	72.0%@1.0uM	0.38uM		
B-1041	70.0%@1.0uM	73.0%@1.0uM		
B-1042	79.0%@1.0uM	12.0%@1.0uM		
B-1043	64.0%@1.0uM	53.0%@1.0uM		
B-1044	94.0%@1.0uM	0.93uM		
B-1045	78.0%@1.0uM	25.0%@1.0uM		
B-1046	72.0%@1.0uM	66.0%@1.0uM		
B-1047	72.0%@1.0uM	58.0%@1.0uM		
B-1048	67.0%@1.0uM	19.0%@1.0uM		
B-1049	67.0%@1.0uM	65.0%@1.0uM		
B-1050	-	0.54uM		
B-1051	68.0%@1.0uM	41%@1.0uM		
B-1052	69.0%@1.0uM	66%@1.0uM		
B-1053	78.0%@1.0uM	0.4uM		
B-1054	79.0%@1.0uM	55.0%@1.0uM		
B-1055	89.0%@1.0uM	63.0%@1.0uM		
B-1056	89.0%@1.0uM	0.76uM		
B-1057	85.0%@1.0uM	0.72uM		
B-1058	0.66uM	43.0%@1.0uM		
B-1059	0.18uM	24.0%@1.0uM		
B-1060	0.11uM	32.0%@1.0uM		
B-1061	0.03uM	19.0%@1.0uM		
B-1062	<0.1uM	26.0%@1.0uM		
B-1063	0.16uM	44.0%@1.0uM		
B-1064	0.39uM	50.0%@1.0uM		
B-1065	0.56uM	40.0%@1.0uM		
B-1066	<0.1uM	39.0%@1.0uM		
B-1067	1.6uM	32.0%@1.0uM		
B-1068	0.48uM	24.0%@1.0uM		
B-1069	0.22uM	27.0%@1.0uM		
B-1070	<0.1uM	44.0%@1.0uM		
B-1071	<0.1uM	48.0%@1.0uM		
B-1072	0.38uM	28.0%@1.0uM		
B-1073	<0.1uM	21.0%@1.0uM		
B-1074	0.23uM	33.0%@1.0uM		
B-1075	0.03uM	29.0%@1.0uM		
B-1076	0.08uM	31.0%@1.0uM		
B-1077	<0.1uM	38.0%@1.0uM		
B-1078	0.26uM	48.0%@1.0uM		
B-1079	<0.1uM	40.0%@1.0uM		
B-1080	0.19uM	28.0%@1.0uM		
B-1081	<0.1uM	37.0%@1.0uM		
B-1082	<0.1uM	54.0%@1.0uM		
B-1083	<0.1uM	23.0%@1.0uM		
B-1084	0.43uM	29.0%@1.0uM		
B-1085	<0.1uM	29.0%@1.0uM		
B-1086	<0.1uM	42.0%@1.0uM		
B-1087	0.05uM	32.0%@1.0uM		
B-1088	0.73uM	49.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1089	<0.1uM	39.0% @ 1.0uM		
B-1090	<0.1uM	90.0% @ 1.0uM		
B-1091	<0.1uM	73.0% @ 1.0uM		
B-1092	0.27uM	85.0% @ 1.0uM		
B-1093	0.33uM	36.0% @ 1.0uM		
B-1094	0.013uM	69.0% @ 1.0uM		
B-1095	<0.1uM	70.0% @ 1.0uM		
B-1096	<0.1uM	32.0% @ 1.0uM		
B-1097	<0.1uM	44.0% @ 1.07uM		
B-1098	<0.1uM	82.0% @ 1.0uM		
B-1099	0.26uM	74.0% @ 1.0uM		
B-1100	0.22uM	56.0% @ 1.0uM		
B-1101	0.026uM	82.0% @ 1.0uM		
B-1102	0.035uM	83.0% @ 1.0uM		
B-1103	0.094uM	90.0% @ 1.0uM		
B-1104	0.12uM	69.0% @ 1.0uM		
B-1105	<0.1uM	84.0% @ 1.0uM		
B-1106	<0.1uM	86.0% @ 1.0uM		
B-1107	0.057uM	84.0% @ 1.0uM		
B-1108	0.22uM	81.0% @ 1.0uM		
B-1109	0.054uM	80.0% @ 1.0uM		
B-1110	0.47uM	64.0% @ 1.0uM		
B-1111	0.19uM	64.0% @ 1.0uM		
B-1112	0.58uM	43.0% @ 1.0uM		
B-1113	<0.1uM	72.0% @ 1.0uM		
B-1114	0.069uM	51.0% @ 1.0uM		
B-1115	0.024uM	89.0% @ 1.0uM		
B-1116	0.41uM	81.0% @ 1.0uM		
B-1117	0.13uM	73.0% @ 1.0uM		
B-1118	0.33uM	91.0% @ 1.0uM		
B-1119	0.35uM	80.0% @ 1.0uM		
B-1120	0.47uM	9.0% @ 1.0uM		
B-1121	3.58uM	29.0% @ 1.0uM		
B-1122	1.84uM	32.0% @ 1.0uM		
B-1123	2.93uM	27.0% @ 1.0uM		
B-1124	1.49uM	52.0% @ 1.0uM		
B-1125	0.56uM	41.0% @ 1.0uM		
B-1126	1.5uM	>1.0uM		
B-1127	0.71uM	7.0% @ 1.0uM		
B-1128	2.55uM	26.0% @ 1.0uM		
B-1129	1.07uM	46.0% @ 1.0uM		
B-1130	0.5uM	29.0% @ 1.0uM		
B-1131	0.076uM	34.0% @ 1.0uM		
B-1132	0.72uM	11.0% @ 1.0uM		
B-1133	0.38uM	33.0% @ 1.0uM		
B-1134	1.71uM	33.0% @ 1.0uM		
B-1135	0.23uM	38.0% @ 1.0uM		
B-1136	1.17uM	40.0% @ 1.0uM		
B-1137	0.038uM	35.0% @ 1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1138	1.82uM	>1.0uM		
B-1139	0.041uM	29.0%@1.0uM		
B-1140	1.68uM	39.0%@1.0uM		
B-1141	2.47uM	32.0%@1.0uM		
B-1142	0.11uM	37.0%@1.0uM		
B-1143	0.17uM	40.0%@1.0uM		
B-1144	0.44uM	72.0%@1.0uM		
B-1145	1.07uM	71.0%@1.0uM		
B-1146	0.47uM	61.0%@1.0uM		
B-1147	0.095uM	53.0%@1.0uM		
B-1148	0.43uM	61.0%@1.0uM		
B-1149	1.55uM	48.0%@1.0uM		
B-1150	0.47uM	75.0%@1.0uM		
B-1151	0.32uM	72.0%@1.0uM		
B-1152	0.73uM	53.0%@1.0uM		
B-1153	2.22uM	52.0%@1.0uM		
B-1154	0.085uM	46.0%@1.0uM		
B-1155	3.22uM	30.0%@1.0uM		
B-1156	0.27uM	78.0%@1.0uM		
B-1157	0.26uM	66.0%@1.0uM		
B-1158	74%@1.0uM	0.68uM	53%@30mpk@-6h	
B-1159	66.0%@1.0uM	1.03uM	60%@30mpk@-6h	
B-1160	79.0%@1.0uM	0.38uM		
B-1161	64.0% <sup>2</sup> 1.0uM	0.93uM	40%@30mpk@-6h	45%@3mpk@-4h
B-1162	79.0%@1.0uM	0.59uM	40%@30mpk@-6h	
B-1163	74.0%@1.0uM	0.37uM		
B-1164	-	0.35uM		
B-1165	66.0%@1.0uM	0.99uM		
B-1166	77.0%@1.0uM	0.39uM	50%@30mpk@-6h	50%@3mpk@-4h
B-1167	70.0%@1.0uM	1.06uM		
B-1168	66.0%@1.0uM	0.63uM		
B-1169	80.0%@1.0uM	0.11uM		
B-1170	82.0%@1.0uM	0.57uM		
B-1171	78.0%@1.0uM	0.23uM		
B-1172	68.0%@1.0uM	1.95uM		
B-1173	65.0%@1.0uM	62%@1.0uM		
B-1174	80.0%@1.0uM	0.86uM		
B-1175	72.0%@1.0uM	1.83uM		
B-1176	67.0%@1.0uM	67.0%@1.0uM		
B-1177	70.0%@1.0uM	1.16uM		
B-1178	92.0%@1.0uM	1.61uM		
B-1179	86.0%@1.0uM	0.41uM		
B-1180	78.0%@1.0uM	0.53uM		
B-1181	79.0%@1.0uM	66%@1.0uM		
B-1182	72.0%@1.0uM	0.65uM		
B-1183	77.0%@1.0uM	0.2uM		
B-1184	69.0%@1.0uM	0.63uM		
B-1185	71.0%@1.0uM	0.79uM		
B-1186	83.0%@1.0uM	60%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1187	76.0%@1.0uM	1.89uM		
B-1188	-	36.0%@1.0uM		
B-1189	68.0%@1.0uM	0.83uM		
B-1190	78.0%@1.0uM	62.0%@1.0uM		
B-1191	74.0%@1.0uM	57.0%@1.0uM		
B-1192	84.0%@1.0uM	0.47uM		
B-1193	69.0%@1.0uM	65.0%@1.0uM		
B-1194	87.0%@1.0uM	0.58uM		
B-1195	52.0%@1.0uM	60.0%@1.0uM		
B-1196	74.0%@1.0uM	68.0%@1.0uM		
B-1197	77.0%@1.0uM	45.0%@1.0uM		
B-1198	92.0%@1.0uM	0.46uM		
B-1199	87.0%@1.0uM	49.0%@1.0uM		
B-1200	95.0%@1.0uM	0.64uM		
B-1201	84.0%@1.0uM	0.51uM		
B-1202	71.0%@1.0uM	58.0%@1.0uM		
B-1203	84.0%@1.0uM	58.0%@1.0uM		
B-1204	68.0%@1.0uM	59.0%@1.0uM		
B-1205	74.0%@1.0uM	46.0%@1.0uM		
B-1206	81.0%@1.0uM	0.34uM		
B-1207	90.0%@1.0uM	58.0%@1.0uM		
B-1208	82.0%@1.0uM	51.0%@1.0uM		
B-1209	86.0%@1.0uM	55.0%@1.0uM		
B-1210	82.0%@1.0uM	57.0%@1.0uM		
B-1211	88.0%@1.0uM	59.0%@1.0uM		
B-1212	90.0%@1.0uM	57.0%@1.0uM		
B-1213	84.0%@1.0uM	0.62uM		
B-1214	76.0%@1.0uM	58.0%@1.0uM		
B-1215	86.0%@1.0uM	0.23uM		
B-1216	88.0%@1.0uM	0.18uM		
B-1217	87.0%@1.0uM	0.46uM		
B-1218	88.0%@1.0uM	76.0%@1.0uM		
B-1219	85.0%@1.0uM	37.0%@1.0uM		
B-1220	81.0%@1.0uM	53.0%@1.0uM		
B-1221	82.0%@1.0uM	44.0%@1.0uM		
B-1222	65.0%@1.0uM	9.0%@1.0uM		
B-1223	80.0%@1.0uM	61.0%@1.0uM		
B-1224	82.0%@1.0uM	74.0%@1.0uM		
B-1225	89.0%@1.0uM	73.0%@1.0uM		
B-1226	89.0%@1.0uM	0.18uM		
B-1227	83.0%@1.0uM	0.22uM		
B-1228	90.0%@1.0uM	0.72uM		
B-1229	87.0%@1.0uM	0.65uM		
B-1230	90.0%@1.0uM	0.25uM		
B-1231	94.0%@1.0uM	0.56uM		
B-1232	81.0%@1.0uM	54.0%@1.0uM		
B-1233	85.0%@1.0uM	0.36uM		
B-1234	89.0%@1.0uM	0.49uM		
B-1235	0.04uM	76.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1236	0.1uM	53.0%@1.0uM		
B-1237	0.22uM	39.0%@1.0uM		
B-1238	0.14uM	16.0%@1.0uM		
B-1239	<0.1uM	38.0%@1.0uM		
B-1240	<0.1uM	59.0%@1.0uM		
B-1241	0.04uM	81.0%@1.0uM		
B-1242	0.08uM	83.0%@1.0uM		
B-1243	0.04uM	47.0%@1.0uM		
B-1244	0.26uM	44.0%@1.0uM		
B-1245	0.49uM	42.0%@1.0uM		
B-1246	0.27uM	40.0%@1.0uM		
B-1247	<0.1uM	58.0%@1.0uM		
B-1248	<0.1uM	68.0%@1.0uM		
B-1249	0.24uM	60.0%@1.0uM		
B-1250	0.14uM	18.0%@1.0uM		
B-1251	0.41uM	38.0%@1.0uM		
B-1252	0.17uM	46.0%@1.0uM		
B-1253	0.15uM	57.0%@1.0uM		
B-1254	0.16uM	68.0%@1.0uM		
B-1255	12.9uM	75.0%@1.0uM		
B-1256	0.12uM	41.0%@1.0uM		
B-1257	1.48uM	40.0%@1.0uM		
B-1258	0.07uM	56.0%@1.0uM		
B-1259	<0.1uM	0.48uM		
B-1260	0.11uM	48.0%@1.0uM		
B-1261	0.74uM	44.0%@1.0uM		
B-1262	<0.1uM	63.0%@1.0uM		
B-1263	1.05uM	57.0%@1.0uM		
B-1264	0.32uM	47.0%@1.0uM		
B-1265	0.43uM	51.0%@1.0uM		
B-1266	<0.1uM	58.0%@1.0uM		
B-1267	<0.1uM	73.0%@1.0uM		
B-1268	<0.1uM	79.0%@1.0uM		
B-1269	0.46uM	84.0%@1.0uM		
B-1270	0.47uM	83.0%@1.0uM		
B-1271	0.13uM	74.0%@1.0uM		
B-1272	0.014uM	38.0%@1.0uM		
B-1273	<0.1uM	36.0%@1.0uM		
B-1274	<0.1uM	41.0%@1.0uM		
B-1275	<0.1uM	50.0%@1.0uM		
B-1276	0.062uM	11.0%@1.0uM		
B-1277	<0.1uM	47.0%@1.0uM		
B-1278	0.12uM	85.0%@1.0uM		
B-1279	<0.1uM	79.0%@1.0uM		
B-1280	0.039uM	83.0%@1.0uM		
B-1281	<0.1uM	85.0%@1.0uM		
B-1282	<0.1uM	75.0%@1.0uM		
B-1283	<0.1uM	64.0%@1.0uM		
B-1284	<0.1uM	75.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1285	0.057uM	80.0%@1.0uM		
B-1286	0.15uM	78.0%21.0uM		
B-1287	0.25uM	55.0%@1.0uM		
B-1288	0.15uM	74.0%@1.0uM		
B-1289	0.73uM	35.0%@1.0uM		
B-1290	0.26uM	75.0%@1.0uM		
B-1291	0.097uM	55.0%@1.0uM		
B-1292	0.01uM	74.0%@1.0uM		
B-1293	0.31uM	48.0%@1.0uM		
B-1294	0.013uM	54.0%@1.0uM		
B-1295	0.079uM	74.0%@1.0uM		
B-1296	0.038uM	48.0%@1.0uM		
B-1297	0.02uM	>1.0uM		
B-1298	0.055uM	20.0%@1.0uM		
B-1299	0.091uM	>1.0uM		
B-1300	0.071uM	18.0%@1.0uM		
B-1301	0.12uM	15.0%@1.0uM		
B-1302	0.023uM	11.0%@1.0uM		
B-1303	0.08uM	>1.0uM		
B-1304	0.11uM	10.0%@1.0uM		
B-1305	0.64uM	9.0%@1.0uM		
B-1306	0.11uM	>1.0uM		
B-1307	0.009uM	16.0%@1.0uM		
B-1308	<0.1uM	>1.0uM		
B-1309	0.045uM	>1.0uM		
B-1310	0.12uM	11.0%@1.0uM		
B-1311	0.05uM	57.0%@1.0uM		
B-1312	0.35uM	>1.0uM		
B-1313	0.035uM	37.0%@1.0uM		
B-1314	0.045uM	24.0%@1.0uM		
B-1315	0.055uM	12.0%@1.0uM		
B-1316	0.026uM	36.0%@1.0uM		
B-1317	0.019uM	9.0%@1.0uM		
B-1318	<0.1uM	1.0%@1.0uM		
B-1319	0.24uM	>1.0uM		
B-1320	0.047uM	43.0%@1.0uM		
B-1321	0.47uM	66.0%@1.0uM		
B-1322	0.12uM	87.0%@1.0uM		
B-1323	0.013uM	85.0%@1.0uM		
B-1324	0.16uM	83.0%@1.0uM		
B-1325	0.27uM	95.0%@1.0uM		
B-1326	0.092uM	84.0%@1.0uM		
B-1327	0.13uM	65.0%@1.0uM		
B-1328	0.032uM	86.0%@1.0uM		
B-1329	0.66uM	54.0%@1.0uM		
B-1330	0.053uM	85.0%@1.0uM		
B-1331	0.004uM	85.0%@1.0uM		
B-1332	0.007uM	81.0%@1.0uM		
B-1333	0.45uM	76.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1334	0.13uM	73.0%@1.0uM		
B-1335	0.097uM	63.0%@1.0uM		
B-1336	0.072uM	83.0%@1.0uM		
B-1337	0.4uM	90.0%@1.0uM		
B-1338	0.18uM	73.0%@1.0uM		
B-1339	0.12uM	67.0%@1.0uM		
B-1340	0.043uM	63.0%@1.0uM		
B-1341	0.42uM	52.0%@1.0uM		
B-1342	0.25uM	59.0%@1.0uM		
B-1343	0.065uM	83.0%@1.0uM		
B-1344	0.014uM	86.0%@1.0uM		
B-1345	0.27uM	73.0%@1.0uM		
B-1346	0.043uM	86.0%@1.0uM		
B-1347	0.021uM	84.0%@1.0uM		
B-1348	0.009uM	69.0%@1.0uM		
B-1349	0.037uM	86.0%@1.0uM		
B-1350	0.019uM	78.0%@1.0uM		
B-1351	0.068uM	78.0%@1.0uM		
B-1352	0.013uM	76.0%@1.0uM		
B-1353	0.062uM	80.0%@1.0uM		
B-1354	0.013uM	83.0%@1.0uM		
B-1355	0.07uM	75.0%@1.0uM		
B-1356	0.059uM	91.0%@1.0uM		
B-1357	0.18uM	84.0%@1.0uM		
B-1358	0.16uM	76.0%@1.0uM		
B-1359	0.005	84.0%@1.0uM		
B-1360	0.11	0.15uM		54%@3mpk@-4h
B-1361	0.03	0.29uM		
B-1362	0.003	0.29uM		
B-1363	0.009	0.28uM	51.0%@30pmk @-6H	53%@3mpk@-4h
B-1364	0.009	0.27uM	53.0%@30mpk@-6.0H	17%@3mpk@-4h
B-1365	0.17	88.0%@1.0uM		
B-1366	0.04	0.27uM		
B-1367	<0.1	0.22uM		
B-1368	0.031	0.33uM	44.0%@30mpk @-	
B-1369	<0.1	0.29uM		
B-1370	<0.1	0.77uM		
B-1371	0.06	83.0%@1.0uM		
B-1372	<0.1	0.41uM	48.0%@30mpk @-	
B-1373	0.016	0.17uM		
B-1374	<0.1	0.28uM		
B-1375	0.01	0.25uM		
B-1376	0.009	0.26uM	3.0%@30mpk @-6H	
B-1377	0.12	5.0uM		
B-1378	0.02	1.04uM		
B-1379	<0.1	0.092uM		
B-1380	<0.1	0.26uM		



Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1381	0.055	0.73uM		
B-1382	<0.1	0.44uM		
B-1383	0.0012	0.15uM		
B-1384	0.57	0.37uM		
B-1385	<0.1	0.11uM		
B-1386	<0.1	0.25uM		
B-1387	<0.1	0.1uM		
B-1388	0.57	1.38uM		
B-1389	0.06	0.57uM		
B-1390	<0.1	71.0%@1.0uM		
B-1391	0.016uM	82.0%@1.0uM		
B-1392	0.059uM	82.0%@1.0uM		
B-1393	3.17uM	80.0%@1.0uM		
B-1394	0.32uM	78.0%@1.0uM		
B-1395	1.48	61.0%@1.0uM		
B-1396	1.55	73.0%@1.0uM		
B-1397	0.92	85.0%@1.0uM		
B-1398	0.67	83.0%@1.0uM		
B-1399	0.14	74.0%@1.0uM		
B-1400	0.024	83.0%@1.0uM		
B-1401	0.033	75.0%@1.0uM		
B-1402	0.12	76.0%@1.0uM		
B-1403	4.54	71%@1.0uM		
B-1404	0.6	70%@1.0uM		
B-1405	0.28	70%@1.0uM		
B-1406	1.39	56.0%@1.0uM		
B-1407	0.4	71.0%@1.0uM		
B-1408	0.27	69.0%@1.0uM		
B-1409	<0.1	72.0%@1.0uM		
B-1410	<0.1	69%@1.0uM		
B-1411	<0.1	81.0%@1.0uM		
B-1412	0.097	80.0%@1.0uM		
B-1413	0.016	78.0%@1.0uM		
B-1414	0.025	83.0%@1.0uM		
B-1415	1.41	79.0%@1.0uM		
B-1416	0.14	81.0%@1.0uM		
B-1417	0.069	69.0%@1.0uM		
B-1418	1.01	82.0%@1.0uM		
B-1419	0.3	84.0%@1.0uM		
B-1420	<0.1	82.0%@1.0uM		
B-1421	0.014	75.0%@1.0uM		
B-1422	0.58	68.0%@1.0uM		
B-1423	1.58	84.0%@1.0uM		
B-1424	0.86	76.0%@1.0uM		
B-1425	0.09	83.0%@1.0uM		
B-1426	0.19	80.0%@1.0uM		
B-1427	<0.1	84.0%@1.0uM		
B-1428	<0.1	86.0%@1.0uM		
B-1429	<0.1	87.0%@1.0uM		

SUBSTITUTE SHEET (RULE 26)

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-1430	0.75uM	35.0% @1.0uM		
B-1431	0.36uM	58.0% @1.0uM		
B-1432	0.11uM	51.0% @1.0uM		
B-1433	0.26uM	21.0% @1.0uM		
B-1434	0.19uM	28.0% @1.0uM		
B-1435	1.8uM	45.0% @1.0uM		
B-1436	1.0uM	20.0% @1.0uM		
B-1437	0.3uM	23.0% @1.0uM		
B-1438	2.01uM	27.0% @1.0uM		
B-1439	1.7uM	17.0% @1.0uM		
B-1440	0.87uM	3.0% @1.0uM		
B-1441	1.95uM	66.0% @1.0uM		
B-1442	1.54uM	18.0% @1.0uM		
B-1443	0.014uM	83.0% @1.0uM		
B-1444	0.3uM	24.0% @1.0uM		
B-1445	0.43uM	27.0% @1.0uM		
B-1446	0.77uM	36.0% @1.0uM		
B-1447	0.5uM	34.0% @1.0uM		
B-1448	1.43uM	22.0% @1.0uM		
B-1449	1.61uM	50.0% @1.0uM		
B-1450	2.1uM	49.0% @1.0uM		
B-1451	2.88uM	50% @1.0uM		
B-1452	2.41uM	47.0% @1.0uM		
B-1453	2.53uM	49.0% @1.0uM		
B-1454	1.6uM	12.0% @1.0uM		
B-1455	1.21uM	8.0% @1.0uM		
B-1456	1.29uM	>1.0uM		
B-1457	0.43uM	43.0% @1.0uM		
B-1458	0.95uM	65.0% @1.0uM		
B-1459	0.67uM	46.0% @1.0uM		
B-1460	0.96uM	29.0% @1.0uM		
B-1461	0.4uM	39.0% @1.0uM		
B-1462	0.22uM	50.0% @1.0uM		
B-1463	2.34uM	26.0% @1.0uM		
B-1464	1.18uM	27.0% @1.0uM		
B-1465	3.23uM	31.0% @1.0uM		
B-1466	1.69uM	>1.0uM		
B-1467	1.22uM	1.0% @1.0uM		
B-1468	1.61uM	10.0% @1.0uM		
B-1469	0.37uM	14.0% @1.0uM		
B-1470	0.6uM	28.0% @1.0uM		
B-1471	0.85uM	25.0% @1.0uM		
B-1472	0.93uM	12.0% @1.0uM		
B-1473	1.24uM	14.0% @1.0uM		
B-1474	1.23uM	31.0% @1.0uM		
B-1475	2.1uM	24.0% @1.0uM		
B-1476	0.047uM	42.0% @1.0uM		
B-1477	2.5uM	34.0% @1.0uM		
B-1478				

	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
Example#				
B-1479				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2270	0.72uM	31%@10.0uM		
B-2271	0.93uM	38%@10.0uM		
B-2272	0.26uM	53.0%@10.0uM		
B-2273	1.92uM	39.0%@10.0uM		
B-2274	0.26uM	59.0%@10.0uM		
B-2275	2.16uM	53.0%@10.0uM		
B-2276	11.5uM	37.0%@10.0uM		
B-2277	14.9uM	44.0%@10.0uM		
B-2278	0.8uM	51.0%@10.0uM		
B-2279	0.32uM	36.0%@10.0uM		
B-2280	0.4uM	57.0%@10.0uM		
B-2281	0.81uM	60.0%@10.0uM		
B-2282	0.91uM	41.0%@10.0uM		
B-2283	0.04uM	53.0%@10.0uM		
B-2284	4.61uM	62.0%@10.0uM		
B-2285	2.29uM	49.0%@10.0uM		
B-2286	0.017uM	0.78uM	25%@30mpk@-1h	
B-2287	2.56uM	61.0%@10.0uM		
B-2288	6.51uM	46.0%@10.0uM		
B-2289	3.0uM	30.0%@10.0uM		
B-2290	2.37uM	59.0%@10.0uM		
B-2291	0.019uM	41%@10.0uM		
B-2292	8.82uM	57.0%@10.0uM		
B-2293	2.11uM	56.0%@10.0uM		
B-2294	1.68uM	50.0%@10.0uM		
B-2295	1.79uM	56.0%@10.0uM		
B-2296	17.3uM	63.0%@10.0uM		
B-2297	3.59uM	57.0%@10.0uM		
B-2298	0.29uM	4.22uM		
B-2299	1.97uM	62.0%@10.0uM		
B-2300	0.07uM	43.0%@10.0uM		
B-2301	0.18uM	44.0%@10.0uM		
B-2302	1.0uM	58.0%@1.0uM		
B-2303	0.011uM	54.0%@10.0uM		
B-2304	1.41uM	50.0%@10.0uM		
B-2305	0.54uM	60.0%@10.0uM		
B-2306	5.88uM	39.0%@10.0uM		
B-2307	2.29uM	69.0%@10.0uM		
B-2308	0.66uM	56.0%@10.0uM		
B-2309	0.29uM	47.0%@10.0uM		

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Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-2310	0.12uM	1.2uM	50%@30mpk@-6h	
B-2311	7.18uM	60.0%@10.0uM		
B-2312	2.93uM	43.0%@10.0uM		
B-2313	42.3uM	58.0%@10.0uM		
B-2314	11.0uM	66.0%@10.0uM		
B-2315	0.49uM	36.0%@10.0uM		
B-2316	0.46uM	58.0%@10.0uM		
B-2317	1.0uM	60.0%@10.0uM		
B-2318	73.0%@10.0uM	25.0%@10.0uM		
B-2319	75.0%@10.0uM	40.0%@10.0uM		
B-2320	44.0%@10.0uM	35.0%@10.0uM		
B-2321	69.0%@10.0uM	27.0%@10.0uM		
B-2322	76.0%@10.0uM	38.0%@10.0uM		
B-2323	69.0%@10.0uM	46.0%@10.0uM		
B-2324	58.0%@10.0uM	36.0%@10.0uM		
B-2325	60.0%@10.0uM	51.0%@10.0uM		
B-2326	76.0%@10.0uM	33.0%@10.0uM		
B-2327	76.0%@10.0uM	23.0%@10.0uM		
B-2328	65.0%@10.0uM	28.0%@10.0uM		
B-2329	72.0%@10.0uM	53.0%@10.0uM		
B-2330	81.0%@10.0uM	37.0%@10.0uM		
B-2331	74.0%@10.0uM	44.0%@10.0uM		
B-2332	70.0%@10.0uM	47.0%@10.0uM		
B-2333	58.0%@10.0uM	36.0%@10.0uM		
B-2334	81.0%@10.0uM	45.0%@10.0uM		
B-2335	82.0%@10.0uM	50.0%@10.0uM		
B-2336	48.0%@10.0uM	35.0%@10.0uM		
B-2337	46.0%@10.0uM	59.0%@10.0uM		
B-2338	73.0%@10.0uM	50.0%@10.0uM		
B-2339	84.0%@10.0uM	>10.0uM		
B-2340	35.0%@10.0uM	12.0%@10.0uM		
B-2341	75.0%@10.0uM	50.0%@10.0uM		
B-2342	83.0%@10.0uM	46.0%@10.0uM		
B-2343	43.0%@10.0uM	27.0%@10.0uM		
B-2344	71.0%@10.0uM	50.0%@10.0uM		
B-2345	64.0%@10.0uM	38.0%@10.0uM		
B-2346	45.0%@10.0uM	48.0%@10.0uM		
B-2347	49.0%@10.0uM	50.0%@10.0uM		
B-2348	76.0%@10.0uM	48.0%@10.0uM		
B-2349	75.0%@10.0uM	27.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2350	38.0% @ 10.0uM	56.0% @ 10.0uM		
B-2351	77.0% @ 10.0uM	1.0% @ 10.0uM		
B-2352	37.0% @ 10.0uM	19.0% @ 10.0uM		
B-2353	38.0% @ 10.0uM	33.0% @ 10.0uM		
B-2354	65.0% @ 10.0uM	25.0% @ 10.0uM		
B-2355	84.0% @ 10.0uM	50.0% @ 10.0uM		
B-2356	77.0% @ 10.0uM	45.0% @ 10.0uM		
B-2357	47.0% @ 10.0uM	41.0% @ 10.0uM		
B-2358	17.0% @ 10.0uM	52.0% @ 10.0uM		
B-2359	76.0% @ 10.0uM	35.0% @ 10.0uM		
B-2360	45.0% @ 10.0uM	>10.0uM		
B-2361	19.0% @ 10.0uM	46.0% @ 10.0uM		
B-2362	60% @ 100.0uM	39.0% @ 10.0uM		
B-2363	44.0% @ 10.0uM	1.0% @ 10.0uM		
B-2364	47.0% @ 10.0uM	4.0% @ 10.0uM		
B-2365	82.0% @ 10.0uM	43.0% @ 10.0uM		
B-2366	70.0% @ 10.0uM	59.0% @ 10.0uM		
B-2367	46.0% @ 10.0uM	40.0% @ 1.0uM		
B-2368	65.0% @ 10.0uM	55.0% @ 10.0uM		
B-2369	32.0% @ 10.0uM	>10.0uM		
B-2370	73% @ 100.0uM	20.0% @ 10.0uM		
B-2371	54.0% @ 10.0uM	36.0% @ 10.0uM		
B-2372	55.0% @ 100.0uM	>10.0uM		
B-2373	50.0% @ 100.0uM	6% @ 10.0uM		
B-2374	35.0% @ 10.0uM	20.0% @ 10.0uM		
B-2375	62.0% @ 100.0uM	>10.0uM		
B-2376	32.0% @ 10.0uM	17.0% @ 10.0uM		
B-2377	34.0% @ 10.0uM	17.0% @ 10.0uM		
B-2378	48.0% @ 10.0uM	61.0% @ 10.0uM		
B-2379	73.0% @ 100.0uM	45.0% @ 1.0uM		
B-2380	81% @ 100.0uM	53.0% @ 10.0uM		
B-2381	68% @ 100.0uM	2.0% @ 10.0uM		
B-2382	51.0% @ 10.0uM	24.0% @ 10.0uM		
B-2383	63.0% @ 10.0uM	35.0% @ 10.0uM		
B-2384	49% @ 100.0uM	10.0% @ 10.0uM		
B-2385	79.0% @ 10.0uM	19.0% @ 10.0uM		
B-2386	38.0% @ 10.0uM	19.0% @ 10.0uM		
B-2387	50.0% @ 100.0uM	>10.0uM		
B-2388	42.0% @ 10.0uM	24.0% @ 10.0uM		
B-2389	39.0% @ 10.0uM	29.0% @ 10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-2390	34.0% @ 10.0uM	27.0% @ 1.0uM		
B-2391	40.0% @ 10.0uM	59.0% @ 10.0uM		
B-2392	63.0% @ 10.0uM	46.0% @ 10.0uM		
B-2393	43.0% @ 10.0uM	>10.0uM		
B-2394	37.0% @ 10.0uM	22.0% @ 10.0uM		
B-2395	32.0% @ 10.0uM	28.0% @ 10.0uM		
B-2396	75.0% @ 10.0uM	>10.0uM		
B-2397	83.0% @ 10.0uM	22.0% @ 10.0uM		
B-2398	55% @ 100.0uM	10.0% @ 10.0uM		
B-2399	69.0% @ 10.0uM	18.0% @ 10.0uM		
B-2400	60.0% @ 10.0uM	40.0% @ 10.0uM		
B-2401	78.0% @ 10.0uM	44.0% @ 10.0uM		
B-2402	43.0% @ 10.0uM	52.0% @ 10.0uM		
B-2403	72% @ 100.0uM	52.0% @ 10.0uM		
B-2404	58% @ 100.0uM	52.0% @ 10.0uM		
B-2405	47% @ 100.0uM	>10.0uM		
B-2406	45.0% @ 10.0uM	24.0% @ 10.0uM		
B-2407	47% @ 100.0uM	27.0% @ 10.0uM		
B-2408	39.0% @ 10.0uM	10.0% @ 10.0uM		
B-2409	78.0% @ 10.0uM	26.0% @ 10.0uM		
B-2410	33.0% @ 10.0uM	32.0% @ 10.0uM		
B-2411	26% @ 100.0uM	13.0% @ 10.0uM		
B-2412	40.0% @ 10.0uM	31.0% @ 10.0uM		
B-2413	75.0% @ 10.0uM	37.0% @ 10.0uM		
B-2414	86.0% @ 10.0uM	38.0% @ 10.0uM		
B-2415	94.0% @ 10.0uM	50.0% @ 10.0uM		
B-2416	85.0% @ 10.0uM	43.0% @ 1.0uM		
B-2417	83.0% @ 10.0uM	18.0% @ 10.0uM		
B-2418	88.0% @ 10.0uM	34.0% @ 10.0uM		
B-2419	86.0% @ 10.0uM	66.0% @ 10.0uM		
B-2420	70.0% @ 10.0uM	34.0% @ 10.0uM		
B-2421	89.0% @ 10.0uM	38.0% @ 10.0uM		
B-2422	90.0% @ 10.0uM	17.0% @ 10.0uM		
B-2423	85.0% @ 10.0uM	>10.0uM		
B-2424	86.0% @ 10.0uM	43.0% @ 10.0uM		
B-2425	79.0% @ 10.0uM	42.0% @ 10.0uM		
B-2426	88.0% @ 10.0uM	53.0% @ 10.0uM		
B-2427	87.0% @ 10.0uM	59.0% @ 10.0uM		
B-2428	82.0% @ 10.0uM	50.0% @ 10.0uM		
B-2429	92.0% @ 10.0uM	32.0% @ 10.0uM		

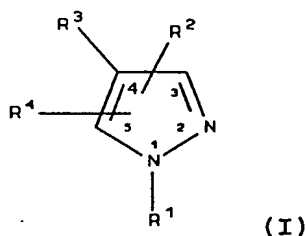
Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-2430	90.0% @ 10.0uM	61.0% @ 10.0uM		
B-2431	85.0% @ 10.0uM	68.0% @ 10.0uM		
B-2432	86.0% @ 10.0uM	40.0% @ 10.0uM		
B-2433	94.0% @ 10.0uM	84.0% @ 10.0uM		
B-2434	92.0% @ 10.0uM	63.0% @ 10.0uM		
B-2435	84.0% @ 10.0uM	4.0% @ 10.0uM		
B-2436	80.0% @ 10.0uM	54.0% @ 10.0uM		
B-2437	82.0% @ 10.0uM	41.0% @ 10.0uM		
B-2438	75.0% @ 10.0uM	40.0% @ 10.0uM		
B-2439	81.0% @ 10.0uM	44.0% @ 10.0uM		
B-2440	77.0% @ 10.0uM	78.0% @ 10.0uM		
B-2441	86.0% @ 10.0uM	46.0% @ 10.0uM		
B-2442	86.0% @ 10.0uM	>10.0uM		
B-2443	84.0% @ 10.0uM	44.0% @ 10.0uM		
B-2444	89.0% @ 10.0uM	7.0% @ 10.0uM		
B-2445	94.0% @ 10.0uM	15.0% @ 10.0uM		
B-2446	90.0% @ 10.0uM	28.0% @ 10.0uM		
B-2447	94.0% @ 10.0uM	>10.0uM		
B-2448	75.0% @ 10.0uM	30.0% @ 10.0uM		
B-2449	86.0% @ 10.0uM	42.0% @ 10.0uM		
B-2450	87.0% @ 10.0uM	46.0% @ 1.0uM		
B-2451	87.0% @ 10.0uM	45.0% @ 10.0uM		
B-2452	89.0% @ 10.0uM	33.0% @ 10.0uM		
B-2453	91.0% @ 10.0uM	>10.0uM		
B-2454	88.0% @ 10.0uM	40.0% @ 10.0uM		
B-2455	87.0% @ 10.0uM	54.0% @ 10.0uM		
B-2456	86.0% @ 10.0uM	53.0% @ 10.0uM		
B-2457	90.0% @ 10.0uM	18.0% @ 10.0uM		
B-2458	83.0% @ 10.0uM	36.0% @ 10.0uM		
B-2459	82.0% @ 10.0uM	81.0% @ 10.0uM		
B-2460	80.0% @ 10.0uM	79.0% @ 10.0uM		
B-2461	67.0% @ 10.0uM	59.0% @ 10.0uM		



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WHAT WE CLAIM IS:

1. A compound of Formula I



5 wherein

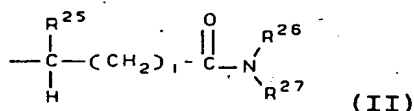
$R^1$  is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxy carbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocycliloxy carbonylalkylene, alkoxy carbonylarylene, aryloxy carbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,

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arylcarbonyloxyarylene, and  
heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



35 wherein:

i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
40 alkylcarbonylalkylene, arylcarbonylalkylene, and  
heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
alkynyl, cycloalkylalkylene, aralkyl,  
alkoxycarbonylalkylene, and alkylaminoalkyl; and

45 R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
cycloalkenylalkylene, cycloalkylarylene,  
cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
50 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
aryloxyarylene, aralkoxyarylene,  
alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
55 alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,  
alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,  
alkylaminoalkylene, arylaminocarbonylalkylene,  
alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,  
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,  
60 arylcarbonylalkylene, alkoxycarbonylarylene,  
aryloxycarbonylarylene, alkylaryloxycarbonylarylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,

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alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxylarylene,  
65 heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
70 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
75 arylthioalkylarylene, and alkylsulfonylarylene groups  
are optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
80 is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups are optionally substituted with one  
85 or more radicals independently selected from alkyl and  
nitro; or

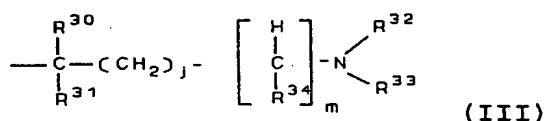
$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
90 radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
95 alkoxycarbonylamino; wherein said aryl,  
heterocyclylalkylene and aryloxyalkylene radicals are  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;

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and

100  $R^2$  is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, heterocyclylalkylamino, aralkylamino, 105 aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocycliloxy, alkylthio, arylthio, heterocyclylthio, carboxy, carboxyalkyl, 110 carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonyl, alkoxycarbonylamino, alkoxycarbonylaminoalkylamino, and heterocyclylsulfonyl; 115 wherein the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and cycloalkenyl groups are optionally substituted with one or more radicals independently selected from halo, keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkyl, 120 epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclylalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, arylsulfonyl, and aralkylsulfonyl; or

125  $R^2$  has the formula:



wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

130  $R^{30}$  and  $R^{31}$  are independently selected from hydrogen,

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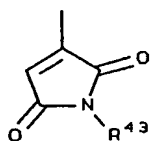
alkyl, aryl, heterocyclyl, aralkyl, heterocyclalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

135  $R^{32}$  is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene;

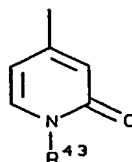
140  $R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ , wherein  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

145  $R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or  $R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and

$R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,



; and



150

(IV)

(V)

wherein  $R^{43}$  is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

155 wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, 160 aralkoxy, heterocyclalkoxy, amino, alkylamino,

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alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxy, carbonyl, aryloxy, carbonyl, heterocyclyloxy, carbonyl, 165 alkoxy, carbonyl, amino, alkoxy, aralkyl, amino, aminosulfinyl, aminosulfonyl, alkylamino, alkylamino, hydroxy, alkylamino, aralkyl, amino, heterocyclyl, alkylamino, aralkyl, heterocyclyl, amino, nitro, alkylamino, carbonyl, alkyl, carbonyl, amino, halo, sulfonyl, amino, alkyl, halo, alkyl, 170 alkyl, carbonyl, hydrazinyl, alkyl, hydrazinyl, aryl, hydrazinyl, or -NR<sup>44</sup>R<sup>45</sup> wherein R<sup>44</sup> is alkyl, carbonyl or amino, and R<sup>45</sup> is alkyl or aralkyl; and

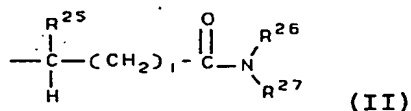
R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein 175 R<sup>4</sup> is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthio, alkylene, arylthio, alkylene, alkylsulfinyl, alkylsulfinyl, alkylene, arylsulfinyl, alkylene, 180 alkylsulfonyl, alkylsulfonyl, alkylene, arylsulfonyl, alkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylamino, carbonyl, arylamino, carbonyl, alkoxy, carbonyl, aryloxy, carbonyl, halo, alkyl, amino, cyano, nitro, alkylamino, arylamino, alkylamino, alkylene, 185 arylamino, alkylene, amino, alkylamino, and hydroxy; provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl ring containing a 2-hydroxy substituent and when R<sup>1</sup> is hydrido; further provided R<sup>2</sup> is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R<sup>4</sup> is 190 hydrido; and further provided R<sup>4</sup> is not methylsulfonylphenyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

2. A compound of Claim 1 wherein

R<sup>1</sup> is selected from hydrido, lower alkyl, lower cycloalkyl, lower alkenyl, lower alkynyl, lower heterocyclyl, lower cycloalkylalkylene, lower haloalkyl, lower hydroxyalkyl, lower aralkyl, lower alkoxyalkyl, lower mercaptoalkyl, lower alkylthioalkylene, amino, lower alkylamino, lower arylamino, lower alkylaminoalkylene, and lower heterocyclylalkylene; or

R<sup>1</sup> has the formula



wherein:

i is 0, 1 or 2; and

R<sup>25</sup> is selected from hydrogen, lower alkyl, lower phenylalkyl, lower heterocyclylalkyl, lower alkoxyalkylene, lower phenoxyalkylene, lower aminoalkyl, lower alkylaminoalkyl, lower phenoxyaminoalkyl, lower alkylcarbonylalkylene, lower phenoxycarbonylalkylene, and lower heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkylalkylene, lower phenylalkyl, lower alkoxycarbonylalkylene, and lower alkylaminoalkyl; and

R<sup>27</sup> is selected from lower alkyl, lower cycloalkyl, lower alkynyl, aryl selected from phenyl, biphenyl and naphthyl, lower heterocyclyl, lower phenylalkyl, lower cycloalkylalkylene, lower cycloalkenylalkylene, lower cycloalkylarylene, lower cycloalkylcycloalkyl, lower heterocyclylalkylene, lower alkylphenylene, lower alkylphenylalkyl, lower phenylalkylphenylene, lower alkylheterocyclyl, lower alkylheterocyclylalkylene, lower alkylheterocyclylphenylene, lower

phenylalkylheterocyclyl, lower alkoxyalkylene, lower  
alkoxyphenylene, lower alkoxyphenylalkyl, lower  
alkoxyheterocyclyl, lower alkoxyalkoxyphenylene, lower  
35 phenoxyphenylene, lower phenylalkoxyphenylene, lower  
alkoxyheterocyclylalkylene, lower phenoxyalkoxyphenylene,  
lower alkoxyacarbonylalkylene, lower  
alkoxyacarbonylheterocyclyl, lower  
alkoxyacarbonylheterocyclylcarbonylalkylene, lower  
40 aminoalkyl, lower alkylaminoalkylene, lower  
phenylaminocarbonylalkylene, lower  
alkoxyphenylaminocarbonylalkylene, lower  
aminocarbonylalkylene, arylaminocarbonylalkylene, lower  
alkylaminocarbonylalkylene, lower phenylcarbonylalkylene,  
45 lower alkoxyacarbonylphenylene, lower  
phenoxyacarbonylphenylene, lower  
alkylphenoxyacarbonylphenylene, lower  
phenylcarbonylphenylene, lower  
alkylphenylcarbonylphenylene, lower  
50 alkoxyacarbonylheterocyclylphenylene, lower  
alkoxyacarbonylalkoxyphenylene, lower  
heterocyclylcarbonylalkylphenylene, lower  
alkylthioalkylene, cycloalkylthioalkylene, lower  
alkylthiophenylene, lower phenylalkylthiophenylene, lower  
55 heterocyclylthiophenylene, lower  
phenylthioalkylphenylene, lower  
phenylsulfonylaminoalkylene, lower  
alkylsulfonylphenylene, lower  
alkylaminosulfonylphenylene; wherein said lower alkyl,  
60 lower cycloalkyl, aryl selected from phenyl, biphenyl and  
naphthyl, lower heterocyclyl, lower phenylalkyl, lower  
heterocyclylalkylene, lower alkylheterocyclylphenylene,  
lower alkoxyphenylene, lower phenoxyphenylene, lower  
phenylaminocarbonylalkylene, lower  
65 phenoxyacarbonylphenylene, lower phenylcarbonylphenylene,  
lower alkylthiophenylene, lower  
heterocyclylthiophenylene, lower



phenylthioalkylphenylene, and lower alkylsulfonylphenylene groups are optionally substituted with one or more radicals independently selected from lower alkyl, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, and cyano; or

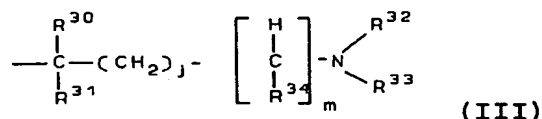
$R^{27}$  is  $-\text{CHR}^{46}\text{R}^{47}$  wherein  $R^{46}$  is lower alkoxy carbonyl, and  $R^{47}$  is selected from lower phenylalkyl, lower phenylalkoxyalkylene, lower heterocyclalkylene, lower alkylheterocyclalkylene, lower alkoxy carbonylalkylene, lower alkylthioalkylene, and lower phenylalkylthioalkylene; wherein said phenylalkyl and heterocycl groups are optionally substituted with one or more radicals independently selected from lower alkyl and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which they are attached form a 4-8 membered ring heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from lower alkyl, aryl selected from phenyl, biphenyl and naphthyl, heterocycl, heterocyclalkylene, lower alkylheterocyclalkylene, lower phenoxyalkylene, lower alkoxyphenylene, lower alkylphenoxyalkylene, lower alkylcarbonyl, lower alkoxy carbonyl, lower phenylalkoxy carbonyl, lower alkylamino and lower alkoxy carbonylamino; wherein said aryl selected from phenyl, biphenyl and naphthyl, lower heterocyclalkylene and lower phenoxyalkylene radicals are optionally substituted with one or more radicals independently selected from halogen, lower alkyl and lower alkoxy; and

$R^2$  is selected from hydrido, halogen, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, lower haloalkyl, lower hydroxyalkyl, 5- or 6-membered heterocycl, lower alkylheterocycl, lower heterocyclalkyl, lower alkylamino, lower alkynylamino, phenylamino, lower heterocyclamino, lower heterocyclalkylamino, lower phenylalkylamino, lower

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- aminoalkyl, lower aminoalkylamino, lower  
 105 alkylaminoalkylamino, lower cycloalkyl, lower alkenyl,  
 lower alkoxy carbonylalkyl, lower cycloalkenyl, lower  
 carboxyalkylamino, lower alkoxy carbonyl, lower  
 heterocyclylcarbonyl, lower alkoxy carbonylheterocyclyl,  
 lower alkoxy carbonylheterocyclylcarbonyl,  
 110 alkoxy carbonylalkyl, lower alkoxyalkylamino, lower  
 alkoxy carbonylaminoalkylamino, lower  
 heterocyclylsulfonyl, lower heterocyclyloxy, and lower  
 heterocyclylthio; wherein the aryl, heterocyclyl,  
 heterocyclylalkyl, cycloalkyl, and cycloalkenyl groups  
 115 are optionally substituted with one or more radicals  
 independently selected from halo, keto, lower alkyl,  
 lower alkynyl, phenyl, 5- or 6-membered heterocyclyl,  
 lower phenylalkyl, lower heterocyclylalkyl, lower  
 epoxyalkyl, carboxy, lower alkoxy, lower aryloxy, lower  
 120 phenylalkoxy, lower haloalkyl, lower alkylamino, lower  
 alkylaminoalkylamino, lower alkynylamino, lower  
 amino(hydroxyalkyl), lower heterocyclylalkylamino, lower  
 alkylcarbonyl, lower alkoxy carbonyl, lower alkylsulfonyl,  
 lower phenylalkylsulfonyl, and phenylsulfonyl; or  
 125  $R^2$  has the formula:



wherein:

- $j$  is 0, 1 or 2; and  
 $m$  is 0;  
 130  $R^{30}$  and  $R^{31}$  are independently selected from hydrogen,  
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,  
 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,  
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and  
 $R^{32}$  is selected from hydrogen, alkyl, aralkyl,  
 135 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,

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aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene; and

140  $R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ ; wherein  $R^{35}$  is selected from alkyl, cycloalkyl, haloalkyl, alkenyl, aryl, heterocyclyl, aralkyl, arylcycloalkyl, cycloalkenylalkylene, heterocyclylalkylene, alkylarylene, alkylheterocyclyl, 145 arylarylene, arylheterocyclyl, alkoxy, alkenoxy, alkoxyalkylene, alkoxyaralkyl, alkoxyarylene, aryloxyalkylene, aralkoxyalkylene, cycloalkyloxyalkylene, alkoxycarbonyl, heterocyclylcarbonyl, alkylcarbonyloxyalkylene, alkylcarbonyloxyarylene, 150 alkoxycarbonylalkylene, alkoxycarbonylarylene, aralkoxycarbonylheterocyclyl, alkylcarbonylheterocyclyl, arylcarbonyloxyalkylarylene, and alkylthioalkylene; wherein said aryl, heterocyclyl, aralkyl, alkylarylene, arylheterocyclyl, alkoxyarylene, aryloxyalkylene, 155 cycloalkoxyalkylene, alkoxycarbonylalkylene, and alkylcarbonylheterocyclyl groups are optionally substituted with one or more radicals independently selected from alkyl, halo, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and cyano; or

160  $R^{35}$  is  $CHR^{48}R^{49}$  wherein  $R^{48}$  is arylsulfonylamino or alkylarylsulfonylamino, and  $R^{49}$  is selected from aralkyl, amino, alkylamino, and aralkylamino; or

$R^{35}$  is  $-NR^{50}R^{51}$  wherein  $R^{50}$  is alkyl, and  $R^{51}$  is aryl; and

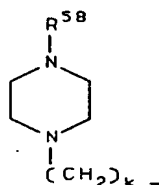
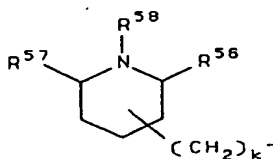
165 wherein  $R^{36}$  is selected from alkyl, haloalkyl, aryl, heterocyclyl, cycloalkylalkylene, alkylarylene, alkenylarylene, arylarylene, aralkyl, aralkenyl, heterocyclylheterocyclyl, carboxyarylene, alkoxyarylene, alkoxycarbonylarylene, alkylcarbonylaminoarylene, 170 alkylcarbonylaminoheterocyclyl, arylcarbonylaminoalkylheterocyclyl, alkylaminoarylene,

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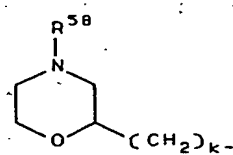
- alkylamino, alkylaminoarylene, alkylsulfonylarylene, alkylsulfonylaralkyl, and arylsulfonylheterocyclyl; wherein said aryl, heterocyclyl, cycloalkylalkylene, aralkyl, alkylcarbonylaminoheterocyclyl, and alkylsulfonylarylene groups are optionally substituted with one or more radicals independently selected from alkyl, halo, hydroxy, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and cyano; and
- 175           wherein  $R^{37}$  is selected from hydrogen and alkyl; and  
              wherein  $R^{38}$  is selected from hydrogen, alkyl, alkenyl, aryl, heterocyclyl, aralkyl, alkylarylene, arylcycloalkyl, arylarylene, cycloalkylalkylene, heterocyclylalkylene, alkylheterocyclylalkylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, aryloxyarylene, arylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkylene, alkoxycarbonylarylene, alkylcarbonylcarbonylalkylene, alkylaminoalkylene, alkylaminoaralkyl, alkylcarbonylaminoalkylene, 185 alkylthioarylene, alkylsulfonylaralkyl, and aminosulfonylaralkyl; wherein said aryl, heterocyclyl, aralkyl, and heterocyclylalkylene groups are optionally substituted with one or more radicals independently selected from alkyl, halo, hydroxy, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and cyano; or
- 195            $R^{38}$  is  $-CR^{52}R^{53}$  wherein  $R^{52}$  is alkoxycarbonyl, and  $R^{53}$  is alkylthioalkylene; or  
               $R^{37}$  and  $R^{38}$  together with the nitrogen atom to which they are attached form a heterocycle; and
- 200            $R^{39}$  and  $R^{40}$  have the same definition as  $R^{26}$  and  $R^{27}$  in claim 1; or  
               $R^2$  is  $-CR^{54}R^{55}$  wherein  $R^{54}$  is phenyl and  $R^{55}$  is hydroxy; or  
               $R^2$  is selected from the group consisting of

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; and



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(VI)

(VII)

(VIII)

wherein

k is an integer from 0 to 3; and

R<sup>56</sup> is hydrogen or lower alkyl; and210 R<sup>57</sup> is hydrogen or lower alkyl; orR<sup>56</sup> and R<sup>57</sup> form a lower alkylene bridge; and

215 R<sup>58</sup> is selected from hydrogen, alkyl, aralkyl, aryl, heterocyclyl, heterocyclylalkyl, alkoxy carbonyl, alkylsulfonyl, aralkylsulfonyl, arylsulfonyl, -C(O)R<sup>59</sup>, -SO<sub>2</sub>R<sup>60</sup>, and -C(O)NHR<sup>61</sup>;

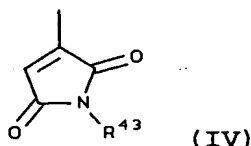
220 wherein R<sup>59</sup> is selected from alkyl, haloalkyl, cycloalkyl, aryl, heterocyclyl, alkylarylene, aralkyl, alkylheterocyclyl, alkoxy, alkenoxy, aralkoxy, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl; wherein said aryl, heterocyclyl, and aralkyl groups are optionally substituted with one or more radicals independently selected from alkyl, halo, hydroxy, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and cyano; and

225 wherein R<sup>60</sup> is selected from alkyl, aryl, heterocyclyl, alkylarylene, alkylheterocyclyl, aralkyl, heterocyclylheterocyclyl, alkoxyarylene, alkylamino, alkylaminoarylene, alkylsulfonylarylene, and arylsulfonylheterocyclyl; wherein said aryl, 230 heterocyclyl, and aralkyl groups are optionally substituted with one or more radicals independently selected from alkyl, halo, hydroxy, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and cyano; and

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wherein  $R^{61}$  is selected from alkyl, aryl, alkylarylene, and alkoxyarylene; wherein said aryl group is optionally substituted with one or more radicals independently selected from alkyl, halo, hydroxy, haloalkyl, alkoxy, haloalkoxy, keto, amino, nitro, and cyano; and

$R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, and



wherein  $R^{43}$  is selected from hydrogen, lower alkyl, lower aminoalkyl, lower alkoxyalkyl, lower alkenoxyalkyl and lower aryloxyalkyl; and

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from lower alkylthio, lower alkylsulfonyl, aminosulfonyl, halo, lower alkyl, lower aralkyl, lower phenylalkenyl, lower phenylheterocyclyl, carboxy, lower alkylsulfinyl, cyano, lower alkoxy carbonyl, aminocarbonyl, lower alkylcarbonylamino, lower haloalkyl, hydroxy, lower alkoxy, amino, lower cycloalkylamino, lower alkylamino, lower alkenylamino, lower alkynylamino, lower aminoalkyl, arylamino, lower aralkylamino, nitro, halosulfonyl, lower alkylcarbonyl, lower alkoxy carbonylamino, lower alkoxyphenylalkylamino, lower alkylaminoalkylamino, lower hydroxyalkylamino, lower heterocyclylamino, lower heterocyclylalkylamino, lower phenylalkylheterocyclylamino, lower alkylaminocarbonyl, lower alkoxyphenylalkylamino, hydrazinyl, lower alkylhydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$  is lower alkylcarbonyl or amino, and  $R^{63}$  is lower alkyl or lower

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265 phenylalkyl; and

R<sup>4</sup> is selected from hydrido, lower cycloalkyl, lower cycloalkenyl, aryl selected from phenyl, biphenyl, and naphthyl, and 5- or 6- membered heterocyclyl; wherein the lower cycloalkyl, lower cycloalkenyl, aryl and 5-10  
270 membered heterocyclyl groups of R<sup>4</sup> are optionally substituted with one or more radicals independently selected from lower alkylthio, lower alkylsulfonyl, lower alkylsulfinyl, halo, lower alkyl, lower alkynyl, lower alkoxy, lower aryloxy, lower aralkoxy, lower  
275 heterocyclyl, lower haloalkyl, amino, cyano, nitro, lower alkylamino, and hydroxy; or  
a pharmaceutically-acceptable salt or tautomer thereof.

3. A compound of Claim 2 wherein

R<sup>1</sup> is selected from hydrido, methyl, ethyl, propyl, isopropyl, tert-butyl, isobutyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl,  
5 dichloromethyl, trichloroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, ethenyl, propenyl, ethynyl, propargyl, 1-propynyl, 2-propynyl, piperidinyl,  
10 piperazinyl, morpholinyl, benzyl, phenylethyl, morpholinylmethyl, morpholinylethyl, pyrrolidinylmethyl, piperazinylmethyl, piperidinylmethyl, pyridinylmethyl, thienylmethyl, methoxymethyl, ethoxymethyl, amino, methylamino, dimethylamino, phenylamino,  
15 methylaminomethyl, dimethylaminomethyl, methylaminoethyl, dimethylaminoethyl, ethylaminoethyl, diethylaminoethyl, cyclopropyl, cyclopentyl, cyclohexyl, cyclohexylmethyl, hydroxymethyl, hydroxyethyl, mercaptomethyl, and methylthiomethyl; and

20 R<sup>2</sup> is selected from hydrido, chloro, fluoro, bromo, methyl, ethyl, propyl, isopropyl, tert-butyl, isobutyl, phenyl, biphenyl, fluoromethyl, difluoromethyl,

trifluoromethyl, chloromethyl, dichloromethyl,  
trichloromethyl, pentafluoroethyl, heptafluoropropyl,  
25 difluoro-chloromethyl, dichloro-fluoromethyl,  
difluoroethyl, difluoropropyl, dichloroethyl,  
dichloropropyl, hydroxymethyl, hydroxyethyl, pyridinyl,  
isothiazolyl, isoxazolyl, thienyl, thiazolyl, oxazolyl,  
pyrimidinyl, quinolyl, isoquinolinyl, imidazolyl,  
30 benzimidazolyl, furyl, pyrazinyl, piperidinyl,  
piperazinyl, morpholinyl, N-methylpiperazinyl,  
methoxycarbonylethyl, ethoxycarbonylethyl, N-methylamino,  
N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-n-  
propylamino, N,N-dimethylamino, N-methyl-N-phenylamino,  
35 N-phenylamino, piperadinylamino, N-benzylamino, N-  
propargylamino, cyclopropyl, cyclobutyl, cyclopentyl,  
cyclohexyl, cyclopropenyl, cyclobutenyl, cyclopentenyl,  
cyclohexenyl, cyclohexadienyl, aminomethyl, aminoethyl,  
aminoethylamino, aminopropylamino, N,N-  
40 dimethylaminoethylamino, N,N-dimethylaminopropylamino,  
morpholinylethylamino, morpholinylpropylamino,  
carboxymethylamino, methoxyethylamino, methoxycarbonyl,  
ethoxycarbonyl, propoxycarbonyl, 1,1-  
dimethylethoxycarbonyl, 1,1-  
45 dimethylethoxycarbonylaminoethylamino, 1,1-  
dimethylethoxycarbonylamino-propylamino,  
piperazinylcarbonyl, and 1,1-  
dimethylethoxycarbonylpiperazinylcarbonyl; wherein the  
aryl, heteroaryl, cycloalkyl and cycloalkenyl groups are  
50 optionally substituted with one or more radicals  
independently selected from fluoro, chloro, bromo, keto,  
methyl, ethyl, isopropyl, tert-butyl, isobutyl, benzyl,  
carboxy, methoxy, ethoxy, phenoxy, benzyloxy,  
trifluoromethyl, fluoromethyl, difluoromethyl,  
55 dimethylamino, methoxycarbonyl, ethoxycarbonyl, and 1,1-  
dimethylethylcarbonyl; or  
R<sup>2</sup> is -CR<sup>54</sup>R<sup>55</sup> wherein R<sup>54</sup> is phenyl and R<sup>55</sup> is hydroxy;  
and



R<sup>3</sup> is selected from pyridinyl, pyrimidinyl, and  
60 purinyl; wherein R<sup>3</sup> is optionally substituted with one or  
more radicals independently selected from methylthio,  
methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,  
aminosulfonyl, methyl, ethyl, isopropyl, tert-butyl,  
isobutyl, cyano, methoxycarbonyl, ethoxycarbonyl,  
65 aminocarbonyl, methylcarbonylamino, trifluoromethyl,  
difluoromethyl, fluoromethyl, trichloromethyl,  
dichloromethyl, chloromethyl, hydroxy,  
fluorophenylmethyl, fluorophenylethyl,  
chlorophenylmethyl, chlorophenylethyl,  
70 fluorophenylethenyl, chlorophenylethenyl,  
fluorophenylpyrazolyl, chlorophenylpyrazolyl, carboxy,  
methoxy, ethoxy, propyloxy, n-butoxy, methylamino,  
ethylamino, dimethylamino, diethylamino, 2-  
methylbutylamino, propargylamino, aminomethyl,  
75 aminoethyl, N-methyl-N-phenylamino, phenylamino,  
diphenylamino, benzylamino, phenethylamino,  
cyclopropylamino, nitro, chlorosulfonyl, amino,  
methylcarbonyl, methoxycarbonylamino,  
ethoxycarbonylamino, methoxyphenylmethylamino, N,N-  
80 dimethylaminoethylamino, hydroxypropylamino,  
hydroxyethylamino, imidazolylethylamino,  
morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,  
piperidinylamino, pyridinylmethylamino,  
phenylmethylpiperidinylamino, phenylmethylamino,  
85 fluorophenylmethylamino, fluorophenylethylamino,  
methylaminocarbonyl, ethylaminocarbonyl, methylcarbonyl,  
methoxyphenylmethylamino, hydrazinyl, 1-methyl-  
hydrazinyl, or -NR<sup>62</sup>R<sup>63</sup> wherein R<sup>62</sup> is methylcarbonyl or  
amino, and R<sup>63</sup> is methyl, ethyl or phenylmethyl; and  
90 R<sup>4</sup> is selected from hydrido, cyclopropyl, cyclobutyl,  
cyclopentyl, cyclohexyl, cyclopropylenyl, cyclobutenyl,  
cyclopentenyl, cyclohexenyl, cyclohexadienyl, phenyl,  
biphenyl, morpholinyl, pyrrolidinyl, piperazinyl,  
piperidinyl, pyridinyl, thienyl, isothiazolyl,

95 isoxazolyl, thiazolyl, oxazolyl, pyrimidinyl, quinolyl,  
isoquinolinyl, imidazolyl, benzimidazolyl, furyl,  
pyrazinyl, dihydropyranyl, dihydropyridinyl,  
dihydrofuryl, tetrahydropyranyl, tetrahydrofuryl,  
benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein  
100 the cycloalkyl, cycloalkenyl, aryl and heterocyclyl  
groups of R<sup>4</sup> are optionally substituted with one or more  
radicals independently selected from methylthio,  
methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,  
methyl, ethyl, isopropyl, tert-butyl, isobutyl, ethynyl,  
105 methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl,  
fluoromethyl, difluoromethyl, amino, cyano, nitro,  
dimethylamino, and hydroxy; or  
a pharmaceutically-acceptable salt or tautomer thereof.

4. A compound of Claim 3 wherein

R<sup>1</sup> is hydrido, methyl, ethyl, propargyl,  
hydroxyethyl, dimethylaminoethyl, diethylaminoethyl or  
morpholinylethyl;

5 R<sup>2</sup> is selected from hydrido, methyl, ethyl, propyl,  
phenyl, trifluoromethyl, methoxycarbonylethyl, N,N-  
dimethylamino, N-phenylamino, piperidinyl, piperazinyl,  
pyridinyl, N-methylpiperazinyl, and piperazinylamino;  
wherein the phenyl, piperidinyl, and pyridinyl groups are  
10 optionally substituted with one or more radicals  
independently selected from fluoro, chloro, bromo,  
methyl, ethyl, and trifluoromethyl;

R<sup>3</sup> is selected from pyridinyl, pyrimidinyl or  
quinolinyl; wherein R<sup>3</sup> is optionally substituted with one  
15 or more radicals independently selected from fluoro,  
bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl,  
benzyl, phenethyl, acetyl, hydroxyl, methoxy,  
dimethylamino, benzylamino, phenethylamino, aminomethyl,  
amino, hydroxy, and methylcarbonyl;

20 R<sup>4</sup> is selected from phenyl, quinolyl, biphenyl,  
pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl,

dihydrobenzofuryl, and benzodioxolyl; wherein the cycloalkyl, cycloalkenyl, aryl and heterocyclyl groups of R<sup>4</sup> are optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; or  
a pharmaceutically-acceptable salt or tautomer thereof.

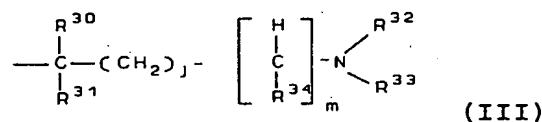
5. A compound of Claim 4 wherein  
R<sup>1</sup> is hydrido or methyl;  
R<sup>2</sup> is selected from hydrido, methyl or ethyl;  
R<sup>3</sup> is selected from pyridinyl, pyrimidinyl or quinolinyl; wherein R<sup>3</sup> is optionally substituted with one or more radicals independently selected from fluoro, bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl, benzyl, phenethyl, acetyl, hydroxyl, methoxy, dimethylamino, benzylamino, phenethylamino, aminomethyl, amino, hydroxy, and methylcarbonyl;

R<sup>4</sup> is selected from phenyl which is optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; or  
a pharmaceutically-acceptable salt or tautomer thereof.

6. A compound of Claim 2 wherein  
R<sup>1</sup> is selected from hydrido, methyl, ethyl, propyl, isopropyl, tert-butyl, isobutyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, ethenyl, propenyl, ethynyl, propargyl, 1-propynyl, 2-propynyl, piperidinyl, piperazinyl, morpholinyl, benzyl, phenylethyl,

morpholinylmethyl, morpholinylethyl, pyrrolidinylmethyl, piperazinylmethyl, piperidinylmethyl, pyridinylmethyl, thienylmethyl, methoxymethyl, ethoxymethyl, amino, methylamino, dimethylamino, phenylamino, methylaminomethyl, dimethylaminomethyl, methylaminoethyl, dimethylaminoethyl, ethylaminoethyl, diethylaminoethyl, cyclopropyl, cyclopentyl, cyclohexyl, cyclohexylmethyl, hydroxymethyl, hydroxyethyl, mercaptomethyl, and methylthiomethyl; and

$R^2$  has the formula:



wherein:

$j$  is 0, 1 or 2; and

$m$  is 0; and

$R^{30}$  and  $R^{31}$  are independently selected from hydrogen and lower alkyl;

$R^{32}$  is selected from hydrogen, lower alkyl, lower phenylalkyl, lower heterocyclalkyl, lower alkoxyalkylene, aryloxyalkylene, aminoalkyl, lower alkylaminoalkyl, lower phenylaminoalkyl, lower alkylcarbonylalkylene, lower phenylcarbonylalkylene, and lower heterocyclalkylcarbonylaminoalkylene;

$R^{33}$  is selected from hydrogen, lower alkyl,  $-C(O)R^{35}$ ,  $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ ;

wherein  $R^{35}$  is selected from lower alkyl, lower cycloalkyl, lower haloalkyl, lower alkenyl, aryl selected from phenyl, biphenyl and naphthyl, lower heterocyclalkyl, lower phenylalkyl, lower phenylcycloalkyl, lower cycloalkenylalkylene, lower heterocyclalkylene, lower alkylphenylene, lower alkylheterocyclalkyl, phenylphenylene, lower phenylheterocyclalkyl, lower alkoxy, lower alkenoxy, lower alkoxyalkylene, lower alkoxyphenylalkyl, lower

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alkoxyphenylene, lower phenoxyalkylene, lower  
phenylalkoxyalkylene, lower cycloalkyloxyalkylene, lower  
45 alkoxy carbonyl, lower heterocyclyl carbonyl, lower  
alkyl carbonyloxyalkylene, lower  
alkyl carbonyloxyphenylene, lower alkoxy carbonylalkylene,  
lower alkoxy carbonylphenylene, lower  
phenylalkoxy carbonyl heterocyclyl, lower  
50 alkyl carbonyl heterocyclyl, lower  
phenyl carbonyloxyalkylphenylene, and lower  
alkylthioalkylene; wherein said aryl selected from  
phenyl, biphenyl and naphthyl, lower heterocyclyl, lower  
phenylalkyl, lower alkylphenylene, lower  
55 phenylheterocyclyl, lower alkoxyphenylene, lower  
phenoxyalkylene, lower cycloalkoxyalkylene, lower  
alkoxy carbonylalkylene, and lower  
alkyl carbonyl heterocyclyl groups are optionally  
substituted with one or more radicals independently  
60 selected from lower alkyl, halo, lower haloalkyl, lower  
alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano;  
or

$R^{35}$  is  $CHR^{48}R^{49}$  wherein  $R^{48}$  is phenylsulfonylamino or  
lower alkylphenylsulfonylamino, and  $R^{49}$  is selected from  
65 lower phenylalkyl, amino, lower alkylamino, and lower  
phenylalkylamino; or

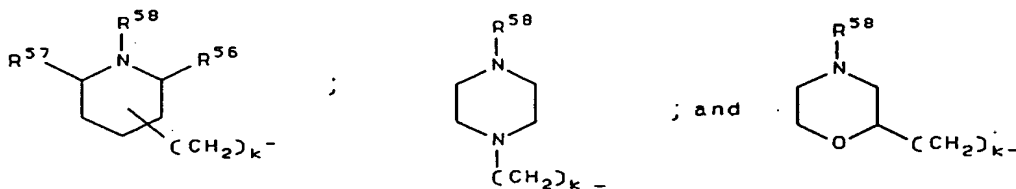
$R^{35}$  is  $-NR^{50}R^{51}$  wherein  $R^{50}$  is lower alkyl, and  $R^{51}$  is  
aryl selected from phenyl, biphenyl and naphthyl; and  
wherein  $R^{36}$  is selected from lower alkyl, lower  
70 haloalkyl, aryl selected from phenyl, biphenyl and  
naphthyl, lower heterocyclyl, lower cycloalkylalkylene,  
lower alkylphenylene, lower alkenylphenylene,  
phenylphenylene, lower phenylalkyl, lower phenylalkenyl,  
lower heterocyclyl heterocyclyl, carboxyphenylene, lower  
75 alkoxyphenylene, lower alkoxy carbonylphenylene, lower  
alkyl carbonylaminophenylene, lower  
alkyl carbonylaminoheterocyclyl, lower  
phenyl carbonylaminoheterocyclyl, lower

alkylaminophenylene, lower alkylamino, lower  
80 alkylaminophenylene, lower alkylsulfonylphenylene, lower  
alkylsulfonylphenylalkyl, and lower  
phenylsulfonylheterocyclyl; wherein said aryl selected  
from phenyl, biphenyl and naphthyl, lower heterocyclyl,  
lower cycloalkylalkylene, lower phenylalkyl, lower  
85 alkylcarbonylaminoheterocyclyl, and lower  
alkylsulfonylphenylene groups are optionally substituted  
with one or more radicals independently selected from  
lower alkyl, halo, hydroxy, lower haloalkyl, lower  
alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano;  
90 and  
wherein  $R^{37}$  is selected from hydrogen and lower  
alkyl; and  
wherein  $R^{38}$  is selected from hydrogen, lower alkyl,  
lower alkenyl, aryl selected from phenyl, biphenyl and  
95 naphthyl, lower heterocyclyl, lower phenylalkyl, lower  
alkylphenylene, lower phenylcycloalkyl, phenylphenylene,  
lower cycloalkylalkylene, lower heterocyclylalkylene,  
lower alkylheterocyclylalkylene, lower  
phenylalkylheterocyclyl, lower alkoxyalkylene, lower  
100 alkoxyphenylene, lower phenoxyphenylene, phenylcarbonyl,  
lower alkoxy carbonyl, lower alkoxy carbonylalkylene, lower  
alkoxy carbonylphenylene, lower  
alkylcarbonylcarbonylalkylene, lower alkylaminoalkylene,  
lower alkylaminophenylalkyl, lower  
105 alkylcarbonylaminoalkylene, lower alkylthiophenylene,  
lower alkylsulfonylphenylalkyl, and lower  
aminosulfonylphenylalkyl; wherein said aryl selected from  
phenyl, biphenyl and naphthyl; lower heterocyclyl, lower  
phenylalkyl, and lower heterocyclylalkylene groups are  
110 optionally substituted with one or more radicals  
independently selected from lower alkyl, halo, hydroxy,  
lower haloalkyl, lower alkoxy, lower haloalkoxy, keto,  
amino, nitro, and cyano; or  
 $R^{38}$  is  $-CR^{52}R^{53}$  wherein  $R_{52}$  is lower alkoxy carbonyl,

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- 115 and  $R_{53}$  is lower alkylthioalkylene; or  
 $R^{37}$  and  $R^{38}$  together with the nitrogen atom to which they are attached form a 4-8 membered ring heterocycle;  
 $R^{39}$  and  $R^{40}$  have the same definition as  $R^{26}$  and  $R^{27}$  in claim 2; or

- 120  $R^2$  is selected from the group consisting of



(VI)

(VII)

(VIII)

wherein

- $k$  is an integer from 0 to 2; and
- 125  $R^{56}$  is hydrogen or lower alkyl; and  
 $R^{57}$  is hydrogen or lower alkyl; and  
 $R^{58}$  is selected from hydrogen, lower alkyl, lower phenylalkyl, aryl selected from phenyl, biphenyl and naphthyl, lower heterocyclyl, lower heterocyclalkyl, lower alkoxy carbonyl, lower alkylsulfonyl, lower phenylalkylsulfonyl, lower phenylsulfonyl,  $-C(O)R^{59}$ ,  $-SO_2R^{60}$ , and  $-C(O)NHR^{61}$ ;
- 130 wherein  $R^{59}$  is selected from lower alkyl, lower haloalkyl, lower cycloalkyl, aryl selected from phenyl, biphenyl and naphthyl, lower heterocyclyl, lower alkylphenylene, lower phenylalkyl, lower alkylheterocyclyl, lower alkoxy, lower alkenoxy, lower phenylalkoxy, lower alkoxyalkylene, lower alkoxyphenylene, lower alkoxyphenylalkyl; wherein said
- 135 aryl selected from phenyl, biphenyl and naphthyl, lower heterocyclyl, and lower phenylalkyl groups are optionally substituted with one or more radicals independently selected from lower alkyl, halo, hydroxy, lower
- 140

haloalkyl, lower alkoxy, lower haloalkoxy, keto, amino,  
145 nitro, and cyano; and  
wherein R<sup>60</sup> is selected from lower alkyl, aryl  
selected from phenyl, biphenyl and naphthyl, lower  
heterocyclyl, lower alkylphenylene, lower  
alkylheterocyclyl, lower phenylalkyl, lower  
150 heterocyclylheterocyclyl, lower alkoxyphenylene, lower  
alkylamino, lower alkylaminophenylene, lower  
alkylsulfonylphenylene, and lower  
phenylsulfonylheterocyclyl; wherein said aryl selected  
from phenyl, biphenyl and naphthyl, lower heterocyclyl,  
155 and lower phenylalkyl groups are optionally substituted  
with one or more radicals independently selected from  
lower alkyl, halo, hydroxy, lower haloalkyl, lower  
alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano;  
and

160 wherein R<sup>61</sup> is selected from lower alkyl, aryl  
selected from phenyl, biphenyl and naphthyl, lower  
alkylphenylene, and lower alkoxyphenylene; wherein said  
aryl group is optionally substituted with one or more  
radicals independently selected from lower alkyl, halo,  
165 hydroxy, lower haloalkyl, lower alkoxy, lower haloalkoxy,  
keto, amino, nitro, and cyano; and

R<sup>3</sup> is selected from pyridinyl, pyrimidinyl, and  
purinyl; wherein R<sup>3</sup> is optionally substituted with one or  
more radicals independently selected from methylthio,  
170 methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,  
aminosulfonyl, methyl, ethyl, isopropyl, tert-butyl,  
isobutyl, cyano, methoxycarbonyl, ethoxycarbonyl,  
aminocarbonyl, methylcarbonylamino, trifluoromethyl,  
difluoromethyl, fluoromethyl, trichloromethyl,  
175 dichloromethyl, chloromethyl, hydroxy,  
fluorophenylmethyl, fluorophenylethyl,  
chlorophenylmethyl, chlorophenylethyl,  
fluorophenylethenyl, chlorophenylethenyl,  
fluorophenylpyrazolyl, chlorophenylpyrazolyl, carboxy,



- 180 methoxy, ethoxy, propyloxy, n-butoxy, methylamino,  
ethylamino, dimethylamino, diethylamino, 2-  
methylbutylamino, propargylamino, aminomethyl,  
aminoethyl, N-methyl-N-phenylamino, phenylamino,  
diphenylamino, benzylamino, phenethylamino,  
185 cyclopropylamino, nitro, chlorosulfonyl, amino,  
methylcarbonyl, methoxycarbonylamino,  
ethoxycarbonylamino, methoxyphenylmethylamino, N,N-  
dimethylaminoethylamino, hydroxypropylamino,  
hydroxyethylamino, imidazolylethylamino,  
190 morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,  
piperidinylamino, pyridinylmethylamino,  
phenylmethylpiperidinylamino, phenylmethylamino,  
fluorophenylmethylamino, fluorophenylethylamino,  
methylaminocarbonyl, ethylaminocarbonyl, methylcarbonyl,  
195 methoxyphenylmethylamino, hydrazinyl, 1-methyl-  
hydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$  is methylcarbonyl or  
amino, and  $R^{63}$  is methyl, ethyl or phenylmethyl; and  
 $R^4$  is selected from hydrido, cyclopropyl, cyclobutyl,  
cyclopentyl, cyclohexyl, cyclopropylenyl, cyclobutenyl,  
200 cyclopentenyl, cyclohexenyl, cyclohexadienyl, phenyl,  
biphenyl, morpholinyl, pyrrolidinyl, piperazinyl,  
piperidinyl, pyridinyl, thienyl, isothiazolyl,  
isoxazolyl, thiazolyl, oxazolyl, pyrimidinyl, quinolyl,  
isoquinolinyl, imidazolyl, benzimidazolyl, furyl,  
205 pyrazinyl, dihydropyranyl, dihydropyridinyl,  
dihydrofuryl, tetrahydropyranyl, tetrahydrofuryl,  
benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein  
the cycloalkyl, cycloalkenyl, aryl and heterocyclyl  
groups of  $R^4$  are optionally substituted with one or more  
210 radicals independently selected from methylthio,  
methylsulfinyl, methylsulfonyl, fluoro, chloro, bromo,  
methyl, ethyl, isopropyl, tert-butyl, isobutyl, ethynyl,  
methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl,  
fluoromethyl, difluoromethyl, amino, cyano, nitro,  
215 dimethylamino, and hydroxy; or

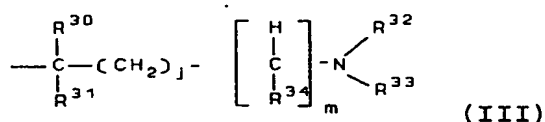
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a pharmaceutically-acceptable salt or tautomer thereof.

7. A compound of Claim 6 wherein

$R^1$  is hydrido, methyl, ethyl, propargyl, hydroxyethyl, dimethylaminoethyl, diethylaminoethyl or morpholinylethyl;

5  $R^2$  has the formula:



wherein:

$j$  is 0, 1 or 2; and

$m$  is 0; and

10  $R^{30}$  is hydrogen; and

$R^{31}$  is selected from hydrogen and lower alkyl; and

$R^{32}$  is selected from hydrogen and lower alkyl; and

$R^{33}$  is selected from lower alkyl,  $-C(O)R^{35}$ ,  $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ ;

15 wherein  $R^{35}$  is selected from lower alkyl, lower

cycloalkyl, phenyl, lower heterocyclyl, lower

alkylphenylene, lower alkoxy, lower alkenoxy, lower

alkoxyalkylene, lower phenoxyalkylene, and lower

20 phenylalkoxyalkylene; wherein said phenyl and lower

phenoxyalkylene groups are optionally substituted with

one or more radicals independently selected from lower

alkyl, halo, and lower haloalkyl; and

wherein  $R^{36}$  is selected from lower alkyl, phenyl,

lower heterocyclyl, lower alkylphenylene,

25 phenylphenylene, lower phenylalkyl, lower

alkylheterocyclyl, lower heterocyclylheterocyclyl, lower

alkoxyphenylene, and lower alkylamino; wherein said

phenyl and lower heterocyclyl groups are optionally

substituted with one or more radicals independently

30 selected from lower alkyl, halo, hydroxy, lower

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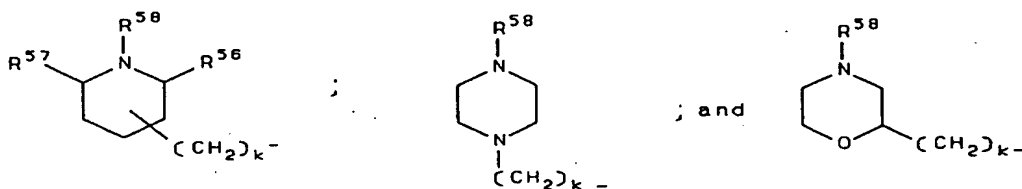
haloalkyl, lower alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano; and

wherein  $R^{37}$  is hydrogen; and

wherein  $R^{38}$  is selected from lower alkyl, phenyl, and  
35 lower alkylphenylene;

wherein  $R^{39}$  and  $R^{40}$  have the same definition as  $R^{26}$  and  $R^{27}$  in claim 2; or

$R^2$  is selected from the group consisting of



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(VI)

(VII)

(VIII)

wherein

$k$  is an integer from 0 or 1; and

$R^{56}$  is hydrogen; and

$R^{57}$  is hydrogen; and

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$R^{58}$  is selected from  $-\text{C}(\text{O})\text{R}^{59}$  and  $-\text{SO}_2\text{R}^{60}$ ;

wherein  $R^{59}$  is selected from lower alkyl, lower cycloalkyl, phenyl, lower alkylphenylene, and lower alkoxyalkylene; wherein said phenyl group is optionally substituted with one or more radicals independently  
50 selected from lower alkyl, halo, hydroxy, lower haloalkyl, lower alkoxy, lower haloalkoxy, keto, amino, nitro, and cyano; and

wherein  $R^{60}$  is selected from lower alkyl; and

$R^3$  is selected from pyridinyl, pyrimidinyl or  
55 quinolinyl; wherein  $R^3$  is optionally substituted with one or more radicals independently selected from fluoro, bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl, benzyl, phenethyl, acetyl, hydroxyl, methoxy, dimethylamino, benzylamino, phenethylamino, aminomethyl,

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- 60 amino, hydroxy, and methylcarbonyl; and  
R<sup>4</sup> is selected from phenyl, quinolyl, biphenyl,  
pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl,  
dihydrobenzofuryl, and benzodioxolyl; wherein the  
cycloalkyl, cycloalkenyl, aryl and heterocyclyl groups of  
65 R<sup>4</sup> are optionally substituted with one or more radicals  
independently selected from methylthio, fluoro, chloro,  
bromo, methyl, ethyl, methoxy, ethoxy, phenoxy,  
benzyloxy, trifluoromethyl, nitro, dimethylamino, and  
hydroxy; or  
70 a pharmaceutically-acceptable salt or tautomer  
thereof.

8. A compound of Claim 7 wherein  
R<sup>1</sup> is hydrido or methyl; and  
R<sup>3</sup> is selected from pyridinyl, pyrimidinyl or  
quinolinyl; wherein R<sup>3</sup> is optionally substituted with one  
5 or more radicals independently selected from fluoro,  
bromo, methyl, cyano, methoxycarbonyl, aminocarbonyl,  
benzyl, phenethyl, acetyl, hydroxyl, methoxy,  
dimethylamino, benzylamino, phenethylamino, aminomethyl,  
amino, hydroxy, and methylcarbonyl; and  
10 R<sup>4</sup> is selected from phenyl which is optionally  
substituted with one or more radicals independently  
selected from methylthio, fluoro, chloro, bromo, methyl,  
ethyl, methoxy, ethoxy, phenoxy, benzyloxy,  
trifluoromethyl, nitro, dimethylamino, and hydroxy; or  
15 a pharmaceutically-acceptable salt or tautomer thereof.

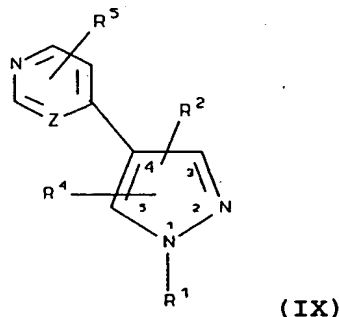
9. A compound of Claim 1 wherein R<sup>1</sup> is hydrido.  
10. A compound of Claim 2 wherein R<sup>1</sup> is hydrido.  
11. A compound of Claim 3 wherein R<sup>1</sup> is hydrido.  
12. A compound of Claim 6 wherein R<sup>1</sup> is hydrido.

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13. A compound of Claim 3 wherein  $R^1$  is methyl or ethyl.
14. A compound of Claim 6 wherein  $R^1$  is methyl or ethyl.
15. A compound of Claim 2 wherein  $R^2$  is hydrido.
16. A compound of Claim 3 wherein  $R^2$  is hydrido.
17. A compound of Claim 2 wherein  $R^4$  is optionally substituted phenyl.
18. A compound of Claim 3 wherein  $R^4$  is optionally substituted phenyl.
19. A compound of Claim 6 wherein  $R^4$  is optionally substituted phenyl.
20. A compound of Claim 2 wherein  $R^1$  and  $R^2$  are selected independently from hydrido, methyl and ethyl.
21. A compound of Claim 3 wherein  $R^1$  and  $R^2$  are selected independently from hydrido, methyl and ethyl
22. A compound of Claim 2 wherein  $R^1$  and  $R^2$  are selected independently from hydrido, methyl and ethyl; and  $R^4$  is optionally substituted phenyl.
23. A compound of Claim 3 wherein  $R^1$  and  $R^2$  are selected independently from hydrido, methyl and ethyl; and  $R^4$  is optionally substituted phenyl.
24. A compound of Formula IX

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wherein

Z represents a carbon atom or a nitrogen atom; and

5        R<sup>1</sup> is selected from hydrido, lower alkyl, lower hydroxyalkyl, lower alkynyl, lower heterocycyl, lower aralkyl, lower aminoalkyl and lower alkylaminoalkyl; and

      R<sup>2</sup> is selected from hydrido, lower alkyl, aryl  
 10        selected from phenyl, biphenyl, and naphthyl, 5- or 6-  
 membered heterocycyl selected from piperidinyl,  
 piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower  
 haloalkyl, lower hydroxyalkyl, lower alkoxy carbonyl,  
 lower alkylamino, lower alkylaminoalkyl, phenylamino,  
 lower aralkyl, lower aralkylamino, lower  
 15        alkylaminoalkylamino, lower aminoalkyl, lower  
 aminoalkylamino, lower alkynylamino, lower  
 heterocyclylamino, lower heterocyclylalkyl, lower  
 heterocyclylalkylamino, lower alkylheterocyclyl, lower  
 carboxycycloalkyl, lower carboxyalkylamino, lower  
 20        alkoxyalkylamino, lower alkoxy carbonylaminoalkylamino,  
 lower heterocyclylcarbonyl, lower  
 alkoxy carbonylheterocyclyl, and lower  
 alkoxy carbonylheterocyclylcarbonyl; wherein the aryl and  
 heteroaryl groups are optionally substituted with one or  
 25        more radicals independently selected from halo, lower

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alkyl, keto, aralkyl, carboxy, lower  
alkylaminoalkylamino, lower alkynylamino, lower  
heterocyclylalkylamino, lower alkylcarbonyl and lower  
alkoxycarbonyl; or

30         $R^2$  is  $-CR^{54}R^{55}$  wherein  $R^{54}$  is phenyl and  $R^{55}$  is hydroxy;  
and

$R^4$  is selected from hydrido, lower cycloalkyl, lower  
cycloalkenyl, lower cycloalkyldienyl, 5- or 6-membered  
heterocyclyl, and aryl selected from phenyl, biphenyl,  
35    naphthyl; wherein  $R^4$  is optionally substituted at a  
substitutable position with one or more radicals  
independently selected from halo, lower alkyl, lower  
alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower  
alkylthio, lower alkylamino, nitro, hydroxy; and

40         $R^5$  is selected from halo, amino, cyano,  
aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower  
aminoalkyl, lower aralkyl, lower aralkyloxy, lower  
aralkylamino, lower alkoxycarbonyl, lower alkylamino,  
lower alkylcarbonyl, lower aralkenyl, lower  
45    arylheterocyclyl, carboxy, lower cycloalkylamino, lower  
alkoxycarbonylamino, lower alkoxyaralkylamino, lower  
alkylaminoalkylamino, lower heterocyclylamino, lower  
heterocyclylalkylamino, lower aralkylheterocyclylamino,  
lower alkylaminocarbonyl, lower alkylcarbonyl, lower  
50    alkoxyaralkylamino, hydrazinyl, and lower  
alkylhydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$  is lower  
alkylcarbonyl or amino, and  $R^{63}$  is lower alkyl or lower  
phenylalkyl; or  
a pharmaceutically-acceptable salt or tautomer thereof.

25. A compound of Claim 24 wherein

$R^1$  is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

$R^2$  is selected from hydrido, methyl, ethyl, propyl,  
5    phenyl, trifluoromethyl, hydroxyethyl,  
methoxycarbonylethyl, ethoxycarbonylethyl, N-methylamino,

**SUBSTITUTESHEET (RULE 26)**

- N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N-phenylamino, aminomethyl, aminoethyl, aminoethylamino, aminopropylamino, propargylamino, benzylamino, dimethylaminopropylamino, morpholinylpropylamino, morpholinylethylamino, piperidinyl, piperazinyl, imidazolyl, morpholinyl, pyridinyl, carboxymethylamino, methoxyethylamino, (1,1-dimethyl)ethylcarbonyl, (1,1-dimethyl)ethylcarbonylaminopropylamino, (1,1-dimethyl)ethylcarbonylaminoethylamino, piperazinylcarbonyl, 1,1-dimethyl-ethylpiperazinylcarbonyl; wherein the phenyl, piperidinyl, piperazinyl, imidazolyl, morpholinyl, and pyridinyl groups are optionally substituted with one or more radicals independently selected from fluoro, chloro, bromo, keto, methyl, ethyl, trifluoromethyl, benzyl, methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-dimethyl)ethoxycarbonyl; and
- R<sup>4</sup> is selected from cyclohexyl, cyclohexenyl, cyclohexadienyl, phenyl, quinolyl, biphenyl, pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein R<sup>4</sup> is optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; and
- R<sup>5</sup> is selected from fluoro, chloro, bromo, methyl, fluorophenylethyl, fluorophenylethenyl, fluorophenylpyrazolyl, cyano, methoxycarbonyl, aminocarbonyl, acetyl, hydroxy, carboxy, methoxy, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxypropylamino, hydroxyethylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, piperidinylamino, pyridinylmethylamino,

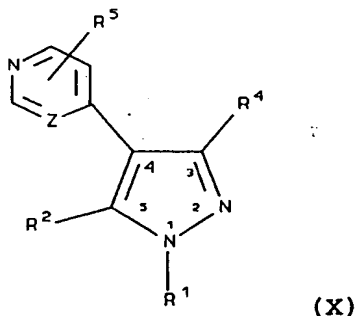


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phenylmethylpiperidinylamino, aminomethyl,  
cyclopropylamino, amino, hydroxy, methylcarbonyl,  
45 ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminocarbonyl,  
methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or -  
NR<sup>62</sup>R<sup>63</sup> wherein R<sup>62</sup> is methylcarbonyl or amino, and R<sup>63</sup> is  
50 methyl or benzyl; or  
a pharmaceutically-acceptable salt or tautomer thereof.

26. A compound of Claim 24 wherein R<sup>1</sup> is hydrido.
27. A compound of Claim 25 wherein R<sup>1</sup> is hydrido.
28. A compound of Claim 24 wherein R<sup>1</sup> is lower alkyl.
29. A compound of Claim 25 wherein R<sup>1</sup> is lower alkyl.
30. A compound of Claim 24 wherein R<sup>2</sup> is hydrido.
31. A compound of Claim 25 wherein R<sup>2</sup> is hydrido.
32. A compound of Claim 24 wherein R<sup>1</sup> and R<sup>2</sup> are selected independently from hydrido, methyl and ethyl.
33. A compound of Claim 25 wherein R<sup>1</sup> and R<sup>2</sup> are selected independently from hydrido, methyl and ethyl.
34. A compound of Claim 25 wherein Z represents a carbon atom.
35. A compound of Formula X

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wherein

Z represents a carbon atom or a nitrogen atom; and

5        R<sup>1</sup> is selected from lower alkyl, lower hydroxyalkyl, lower alkynyl, lower aminoalkyl and lower alkylaminoalkyl; and

      R<sup>2</sup> is selected from hydrido, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, 5- or 6-  
 10    membered heterocyclyl selected from piperidinyl, piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxycarbonyl, lower alkylamino, lower alkylaminoalkyl, phenylamino, lower aralkyl, lower aralkylamino, lower  
 15    alkylaminoalkylamino, lower aminoalkyl, lower aminoalkylamino, lower alkynylamino, lower heterocyclylamino, lower heterocyclylalkyl, lower heterocyclylalkylamino, lower alkylheterocyclyl, lower carboxycycloalkyl, lower carboxyalkylamino, lower  
 20    alkoxyalkylamino, lower alkoxycarbonylaminoalkylamino, lower heterocyclylcarbonyl, lower alkoxycarbonylheterocyclyl, and lower alkoxycarbonylheterocyclylcarbonyl; wherein the aryl and heteroaryl groups are optionally substituted with one or  
 25    more radicals independently selected from halo, lower

**SUBSTITUTESHEET (RULE 26)**

alkyl, keto, aralkyl, carboxy, lower  
alkylaminoalkylamino, lower alkynylamino, lower  
heterocyclylalkylamino, lower alkylcarbonyl and lower  
alkoxycarbonyl; or

30  $R^2$  is  $-CR^{54}R^{55}$  wherein  $R^{54}$  is phenyl and  $R^{55}$  is hydroxy;  
and

$R^4$  is selected from 5- or 6-membered heteroaryl, and  
aryl selected from phenyl, biphenyl, and naphthyl;  
wherein  $R^4$  is optionally substituted with one or more  
35 radicals independently selected from halo, lower alkyl,  
lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl,  
lower alkylthio, lower alkylamino, nitro, hydroxy; and

$R^5$  is selected from halo, amino, cyano,  
aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower  
40 aminoalkyl, lower aralkyl, lower aralkyloxy, lower  
aralkylamino, lower alkoxycarbonyl, lower alkylamino,  
lower alkylcarbonyl, lower aralkenyl, lower  
arylheterocyclyl, carboxy, lower cycloalkylamino, lower  
alkoxycarbonylamino, lower alkoxyaralkylamino, lower  
45 alkylaminoalkylamino, lower heterocyclylamino, lower  
heterocyclylalkylamino, lower aralkylheterocyclylamino,  
lower alkylaminocarbonyl, lower alkylcarbonyl, lower  
alkoxyaralkylamino, hydrazinyl, and lower  
alkylhydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$  is lower  
50 alkylcarbonyl or amino, and  $R^{63}$  is lower alkyl or lower  
phenylalkyl; or  
a pharmaceutically-acceptable salt or tautomer thereof.

36. A compound of Claim 35 wherein

55  $R^1$  is selected from methyl, ethyl, hydroxyethyl and  
propargyl; and

$R^2$  is selected from methyl, ethyl, propyl, phenyl,  
trifluoromethyl, hydroxyethyl, methoxycarbonyl ethyl,  
ethoxycarbonyl ethyl, N-methylamino, N,N-dimethylamino, N-  
60 ethylamino, N,N-diethylamino, N-propylamino, N-  
phenylamino, aminomethyl, aminoethyl, aminoethylamino,

aminopropylamino, propargylamino, benzylamino,  
piperadinylamino, dimethylaminoethylamino,  
dimethylaminopropylamino, morpholinylpropylamino,  
65 morpholinylethylamino, piperidinyl, piperazinyl,  
imidazolyl, morpholinyl, pyridinyl, N-methylpiperazinyl,  
carboxymethylamino, methoxyethylamino, (1,1-  
dimethyl)ethylcarbonyl, (1,1-  
dimethyl)ethylcarbonylamino, (1,1-  
70 dimethyl)ethylcarbonylaminoethylamino,  
piperazinylcarbonyl, and 1,1-dimethyl-  
ethylpiperazinylcarbonyl; wherein the phenyl,  
piperidinyl, piperazinyl, imidazolyl, morpholinyl, and  
pyridinyl groups are optionally substituted with one or  
75 more radicals independently selected from fluoro, chloro,  
bromo, keto, methyl, ethyl, trifluoromethyl, benzyl,  
methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-  
dimethyl)ethoxycarbonyl; and

R<sup>4</sup> is selected from phenyl, quinolyl, biphenyl,  
80 pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl,  
dihydrobenzofuryl, and benzodioxolyl; wherein R<sup>4</sup> is  
optionally substituted with one or more radicals  
independently selected from methylthio, fluoro, chloro,  
bromo, methyl, ethyl, methoxy, ethoxy, phenoxy,  
85 benzyloxy, trifluoromethyl, nitro, dimethylamino, and  
hydroxy; and

R<sup>5</sup> is selected from fluoro, chloro, bromo, methyl,  
fluorophenylethyl, fluorophenylethenyl,  
fluorophenylpyrazolyl, cyano, methoxycarbonyl,  
90 aminocarbonyl, acetyl, hydroxy, carboxy, methoxy,  
methylamino, dimethylamino, 2-methylbutylamino,  
ethylamino, dimethylaminoethylamino, hydroxypropylamino,  
hydroxyethylamino, propargylamino, imidazolylamino,  
morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,  
95 piperidinylamino, pyridinylmethylamino,  
phenylmethylpiperidinylamino, aminomethyl,  
cyclopropylamino, amino, hydroxy, methylcarbonyl,

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ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
100 fluorophenylethylamino, methylaminocarbonyl,  
methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or -  
NR<sup>62</sup>R<sup>63</sup> wherein R<sup>62</sup> is methylcarbonyl or amino, and R<sup>63</sup> is  
methyl or benzyl; or  
a pharmaceutically-acceptable salt or tautomer thereof.

37. A compound of Claim 35 wherein R<sup>1</sup> is lower alkyl.

38. A compound of Claim 36 wherein R<sup>1</sup> is lower alkyl.

39. A compound of Claim 35 wherein R<sup>2</sup> is hydrido.

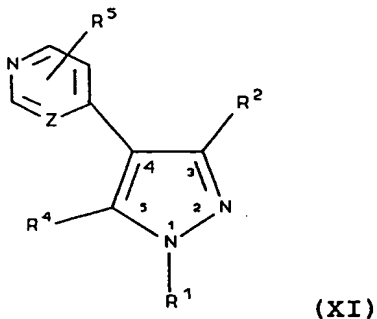
40. A compound of Claim 36 wherein R<sup>2</sup> is hydrido.

41. A compound of Claim 35 wherein R<sup>1</sup> is methyl or  
ethyl, and R<sup>2</sup> is selected from hydrido, methyl and ethyl.

42. A compound of Claim 36 wherein R<sup>1</sup> is methyl or  
ethyl, and R<sup>2</sup> is selected from hydrido, methyl and ethyl.

43. A compound of Claim 35 wherein Z represents a  
carbon atom.

44. A compound of Formula XI



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wherein

Z represents a carbon atom or a nitrogen atom; and

5           R<sup>1</sup> is selected from lower alkyl, lower hydroxyalkyl, lower alkynyl, lower aminoalkyl and lower alkylaminoalkyl; and

          R<sup>2</sup> is selected from hydrido, lower alkyl, aryl selected from phenyl, biphenyl, and naphthyl, 5- or 6-  
10   membered heterocyclyl selected from piperidinyl, piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxycarbonyl, lower alkylamino, lower alkylaminoalkyl, phenylamino, lower aralkyl, lower aralkylamino, lower  
15   alkylaminoalkylamino, lower aminoalkyl, lower aminoalkylamino, lower alkynylamino, lower heterocyclylamino, lower heterocyclylalkyl, lower heterocyclylalkylamino, lower alkylheterocyclyl, lower carboxycycloalkyl, lower carboxyalkylamino, lower  
20   alkoxyalkylamino, lower alkoxycarbonylaminoalkylamino, lower heterocyclylcarbonyl, lower alkoxycarbonylheterocyclyl, and lower alkoxycarbonylheterocyclylcarbonyl; wherein the aryl and heteroaryl groups are optionally substituted with one or  
25   more radicals independently selected from halo, lower alkyl, keto, aralkyl, carboxy, lower alkylaminoalkylamino, lower alkynylamino, lower heterocyclylalkylamino, lower alkylcarbonyl and lower alkoxycarbonyl; or

30           R<sup>2</sup> is -CR<sup>54</sup>R<sup>55</sup> wherein R<sup>54</sup> is phenyl and R<sup>55</sup> is hydroxy; and

          R<sup>4</sup> is selected from 5- or 6-membered heteroaryl, and aryl selected from phenyl, biphenyl, and naphthyl; wherein R<sup>4</sup> is optionally substituted with one or more  
35   radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, hydroxy; and

          R<sup>5</sup> is selected from halo, amino, cyano,

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aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower  
40 aminoalkyl, lower aralkyl, lower aralkyloxy, lower  
aralkylamino, lower alkoxycarbonyl, lower alkylamino,  
lower alkylcarbonyl, lower aralkenyl, lower  
arylheterocyclyl, carboxy, lower cycloalkylamino, lower  
alkoxycarbonylamino, lower alkoxyaralkylamino, lower  
45 alkylaminoalkylamino, lower heterocyclylamino, lower  
heterocyclylalkylamino, lower aralkylheterocyclylamino,  
lower alkylaminocarbonyl, lower alkylcarbonyl, lower  
alkoxyaralkylamino, hydrazinyl, and lower  
alkylhydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$  is lower  
50 alkylcarbonyl or amino, and  $R^{63}$  is lower alkyl or lower  
phenylalkyl; or  
a pharmaceutically-acceptable salt or tautomer thereof.

45. A compound of Claim 44 wherein

$R^1$  is selected from methyl, ethyl, hydroxyethyl and  
propargyl; and

$R^2$  is selected from methyl, ethyl, propyl, phenyl,  
5 trifluoromethyl, hydroxyethyl, methoxycarbonyl ethyl,  
ethoxycarbonyl ethyl, N-methylamino, N,N-dimethylamino, N-  
ethylamino, N,N-diethylamino, N-propylamino, N-  
phenylamino, aminomethyl, aminoethyl, aminoethylamino,  
aminopropylamino, propargylamino, benzylamino,  
10 dimethylaminopropylamino, morpholinylpropylamino,  
morpholinylethylamino, piperidinyl, piperazinyl,  
imidazolyl, morpholinyl, pyridinyl, carboxymethylamino,  
methoxyethylamino, (1,1-dimethyl)ethylcarbonyl, (1,1-  
dimethyl)ethylcarbonylamino propylamino, (1,1-  
15 dimethyl)ethylcarbonylamino ethylamino,  
piperazinylcarbonyl, 1,1-dimethyl-  
ethylpiperazinylcarbonyl; wherein the phenyl,  
piperidinyl, piperazinyl, imidazolyl, morpholinyl, and  
pyridinyl groups are optionally substituted with one or  
20 more radicals independently selected from fluoro, chloro,  
bromo, keto, methyl, ethyl, trifluoromethyl, benzyl,

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methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-dimethyl)ethoxycarbonyl;

R<sup>4</sup> is selected from phenyl, quinolyl, biphenyl, pyridinyl, thienyl, furyl, dihydropyranyl, benzofuryl, dihydrobenzofuryl, and benzodioxolyl; wherein R<sup>4</sup> is optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; and

R<sup>5</sup> is selected from fluoro, chloro, bromo, methyl, fluorophenylethyl, fluorophenylethenyl, fluorophenylpyrazolyl, cyano, methoxycarbonyl, aminocarbonyl, acetyl, hydroxy, carboxy, methoxy, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxypropylamino, hydroxyethylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, piperidinylamino, pyridinylmethylamino, phenylmethylpiperidinylamino, aminomethyl, cyclopropylamino, amino, hydroxy, methylcarbonyl, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminocarbonyl, methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or -NR<sup>62</sup>R<sup>63</sup> wherein R<sup>62</sup> is methylcarbonyl or amino, and R<sup>63</sup> is methyl or benzyl; or a pharmaceutically-acceptable salt or tautomer thereof.

46. A compound of Claim 44 wherein R<sup>1</sup> is lower alkyl.

47. A compound of Claim 45 wherein R<sup>1</sup> is lower alkyl.

48. A compound of Claim 44 wherein R<sup>2</sup> is hydrido.

49. A compound of Claim 45 wherein R<sup>2</sup> is hydrido.

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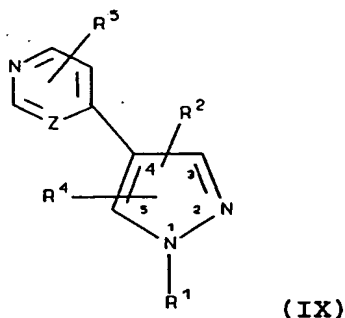
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50. A compound of Claim 44 wherein  $R^1$  is methyl or ethyl, and  $R^2$  is selected from hydrido, methyl and ethyl.

51. A compound of Claim 45 wherein  $R^1$  is methyl or ethyl, and  $R^2$  is selected from hydrido, methyl and ethyl.

52. A compound of Claim 44 wherein Z represents a carbon atom.

53. A compound of Formula IX



wherein

5        Z represents a carbon atom or a nitrogen atom; and  
       $R^1$  is selected from hydrido, lower alkyl, lower hydroxyalkyl, lower alkynyl, lower aminoalkyl and lower alkylaminoalkyl; and

$R^2$  is selected from hydrido, lower alkyl, aryl  
10        selected from phenyl, biphenyl, and naphthyl, 5- or 6-  
      membered heterocyclyl selected from piperidinyl,  
      piperazinyl, imidazolyl, pyridinyl and morpholinyl, lower  
      haloalkyl, lower hydroxyalkyl, lower alkoxycarbonyl,  
      lower alkylamino, lower alkylaminoalkyl, phenylamino,  
      lower aralkyl, lower aralkylamino, lower  
15        alkylaminoalkylamino, lower aminoalkyl, lower

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- aminoalkylamino, lower alkynylamino, lower heterocyclylamino, lower heterocyclylalkyl, lower heterocyclylalkylamino, lower alkylheterocyclyl, lower carboxycycloalkyl, lower carboxyalkylamino, lower  
20 alkoxyalkylamino, lower alkoxycarbonylaminoalkylamino, lower heterocyclylcarbonyl, lower alkoxycarbonylheterocyclyl, and lower alkoxycarbonylheterocyclylcarbonyl; wherein the aryl and heteroaryl groups are optionally substituted with one or  
25 more radicals independently selected from halo, lower alkyl, keto, aralkyl, carboxy, lower alkylaminoalkylamino, lower alkynylamino, lower heterocyclylalkylamino, lower alkylcarbonyl and lower alkoxycarbonyl; or  
30  $R^2$  is  $-CR^{54}R^{55}$  wherein  $R^{54}$  is phenyl and  $R^{55}$  is hydroxy; and  
 $R^4$  is phenyl that is optionally substituted with one or more radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower  
35 haloalkyl, lower alkylthio, lower alkylamino, nitro, hydroxy; and  
 $R^5$  is selected from halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower  
40 aralkylamino, lower alkoxycarbonyl, lower alkylamino, lower alkylcarbonyl, lower aralkenyl, lower arylheterocyclyl, carboxy, lower cycloalkylamino, lower alkoxycarbonylamino, lower alkoxyaralkylamino, lower alkylaminoalkylamino, lower heterocyclylamino, lower  
45 heterocyclylalkylamino, lower aralkylheterocyclylamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$  is lower alkylcarbonyl or amino, and  $R^{63}$  is lower alkyl or lower  
50 phenylalkyl; or  
a pharmaceutically-acceptable salt or tautomer

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thereof.

54. A compound of Claim 53 wherein

$R^1$  is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl;

$R^2$  is selected from methyl, ethyl, propyl, phenyl, trifluoromethyl, hydroxyethyl, methoxycarbonyl-ethyl, ethoxycarbonyl-ethyl, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N-phenylamino, aminomethyl, aminoethyl, aminoethylamino, aminopropylamino, propargylamino, benzylamino, dimethylaminopropylamino, morpholinylpropylamino, morpholinylethylamino, piperidinyl, piperazinyl, imidazolyl, morpholinyl, pyridinyl, carboxymethylamino, methoxyethylamino, (1,1-dimethyl)ethylcarbonyl, (1,1-dimethyl)ethylcarbonylamino, (1,1-dimethyl)ethylcarbonylaminoethylamino, piperazinylcarbonyl, 1,1-dimethyl-ethylpiperazinylcarbonyl; wherein the phenyl, piperidinyl, piperazinyl, imidazolyl, morpholinyl, and pyridinyl groups are optionally substituted with one or more radicals independently selected from fluoro, chloro, bromo, keto, methyl, ethyl, trifluoromethyl, benzyl, methoxy, methoxycarbonyl, ethoxycarbonyl and (1,1-dimethyl)ethoxycarbonyl;

$R^4$  is phenyl that is optionally substituted with one or more radicals independently selected from methylthio, fluoro, chloro, bromo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; and

$R^5$  is selected from fluoro, chloro, bromo, methyl, fluorophenylethyl, fluorophenylethenyl, fluorophenylpyrazolyl, cyano, methoxycarbonyl, aminocarbonyl, acetyl, hydroxy, carboxy, methoxy, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxypropylamino,

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- 35 hydroxyethylamino, imidazolylamino,  
morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino,  
piperidinylamino, pyridinylmethylamino,  
phenylmethylpiperidinylamino, aminomethyl,  
cyclopropylamino, amino, hydroxy, methylcarbonyl,  
40 ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminocarbonyl,  
methylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, or -  
NR<sup>62</sup>R<sup>63</sup> wherein R<sup>62</sup> is methylcarbonyl or amino, and R<sup>63</sup> is  
45 methyl or benzyl; or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

55. A compound of Claim 53 wherein R<sup>1</sup> is hydrido or lower alkyl.

56. A compound of Claim 54 wherein R<sup>1</sup> is hydrido or lower alkyl.

57. A compound of Claim 53 wherein R<sup>1</sup> is hydrido.

58. A compound of Claim 54 wherein R<sup>1</sup> is hydrido.

59. A compound of Claim 53 wherein R<sup>2</sup> is hydrido.

60. A compound of Claim 54 wherein R<sup>2</sup> is hydrido.

61. A compound of Claim 53 wherein R<sup>4</sup> is phenyl substituted with one or more fluoro, chloro or bromo.

62. A compound of Claim 54 wherein R<sup>4</sup> is phenyl substituted with one or more fluoro, chloro or bromo.

63. A compound of Claim 53 wherein R<sup>1</sup> and R<sup>2</sup> are selected independently from hydrido, methyl and ethyl.

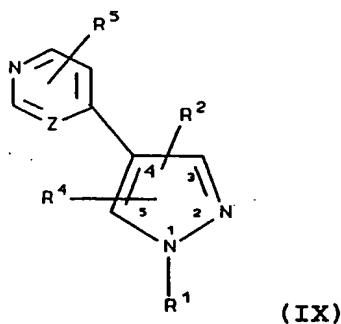
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64. A compound of Claim 54 wherein  $R^1$  and  $R^2$  are selected independently from hydrido, methyl and ethyl.

65. A compound of Claim 53 wherein Z represents a carbon atom.

66. A compound of Formula IX



wherein

Z represents a carbon atom or a nitrogen atom; and

5  $R^1$  is selected from hydrido, lower alkyl, lower hydroxyalkyl and lower alkynyl; and

$R^2$  is selected from hydrido and lower alkyl; and

10  $R^4$  is selected from phenyl and benzodioxolyl; wherein phenyl is optionally substituted with one or more halo radicals; and

$R^5$  is selected from hydrido, halo and alkylhydrazinyl; or a pharmaceutically-acceptable salt or tautomer thereof.

67. A compound of Claim 66 wherein

Z represents a carbon atom; and

$R^1$  is selected from hydrido, methyl, hydroxyethyl, propargyl; and

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5           R<sup>2</sup> is hydrido; and

          R<sup>4</sup> is selected from phenyl and benzodioxolyl; wherein phenyl is optionally substituted with one or more radicals independently selected from chloro, fluoro and bromo; and

10          R<sup>5</sup> is selected from hydrido, fluoro, and 1-methylhydrazinyl; or

          a pharmaceutically-acceptable salt or tautomer thereof.

68. A compound of Claim 67 wherein

          Z represents a carbon atom; and

          R<sup>1</sup> is selected from hydrido and methyl; and

          R<sup>2</sup> is hydrido; and

5           R<sup>4</sup> is selected from phenyl that is optionally substituted with one or more radicals independently selected from chloro, fluoro and bromo; and

          R<sup>5</sup> is selected from hydrido and fluoro; or  
          a pharmaceutically-acceptable salt or tautomer thereof.

69. A compound of Claim 1 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of

5           4-[5-(3-fluoro-4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;

          4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;

          4-[5-methyl-3-(2-methylphenyl)-1H-pyrazol-4-yl]pyridine;

          4-[3-(4-fluorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;

          4-[5-methyl-3-(4-methylphenyl)-1H-pyrazol-4-yl]pyridine;

10          4-[5-methyl-3-[4-(methylthio)phenyl]-1H-pyrazol-4-yl]pyridine;

          4-[3-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;

          4-[3-methyl-5-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;

15          4-[5-(2,5-dimethylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;

          4-[5-(1,3-benzodioxol-5-yl)-3-methyl-1H-pyrazol-4-

- yl]pyridine;  
4-[3-methyl-5-(4-phenoxyphenyl)-1H-pyrazol-4-yl]pyridine;  
4-[5-[(1,1'-biphenyl)-4-yl]-3-methyl-1H-pyrazol-4-  
20 yl]pyridine;  
4-[3-methyl-5-[3-(phenoxyphenyl)-1H-pyrazol-4-  
yl]pyridine;  
4-[3-methyl-5-[3-(phenylmethoxy)phenyl]-1H-pyrazol-4-  
yl]pyridine;  
25 4-[3-methyl-5-[2-(phenylmethoxy)phenyl]-1H-pyrazol-4-  
yl]pyridine;  
2-[3-methyl-4-(4-pyridinyl)-1H-pyrazol-4-yl]phenol;  
3-[3-methyl-4-(4-pyridinyl)-1H-pyrazol-4-yl]phenol;  
1-hydroxy-4-(3-methyl-5-phenyl-1H-pyrazol-4-  
30 yl]pyridinium;  
5-(4-fluorophenyl)-N,N-dimethyl-4-(4-pyridinyl)-1H-  
pyrazol-3-amine;  
5-(4-fluorophenyl)-N-phenyl-4-(4-pyridinyl)-1H-pyrazol-3-  
amine; 4-[5-(4-fluorophenyl)-3-phenyl-1H-pyrazol-4-  
35 yl]pyridine;  
4-[5-(3-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-4-  
yl]pyridine; 4-[3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-  
pyrazol-5-yl]pyridine;  
4-(5-cyclohexyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
40 4-[5-(3-fluoro-5-methoxyphenyl)-3-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[5-(3-methylphenyl)-3-propyl-1H-pyrazol-4-yl]pyridine;  
4-[(3-methyl-5-phenyl-1H-pyrazol-4-yl)methyl]pyridine;  
4-[3,5-bis(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;  
45 4-[4-methyl-2-(2-trifluorophenyl)-1H-pyrazol-4-  
yl]pyridine;  
4-[3-(2-chlorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-methyl-3-(2,4-dimethylphenyl)-1H-pyrazol-4-  
yl]pyridine;  
50 4-[5-(4-chlorophenyl)-1,3-dimethyl-1H-pyrazol-4-  
yl]pyridine;  
4-[3-(3-fluoro-2-methylphenyl)-5-methyl-1H-pyrazol-4-

- yl]pyridine;  
4-[3-(3,5-dimethylphenyl)-5-methyl-1H-pyrazol-4-  
55 yl]pyridine;  
4-[3-(3,5-dimethoxyphenyl)-5-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[5-methyl-3-(3-nitrophenyl)-1H-pyrazol-4-yl]pyridine;  
N,N-dimethyl-4-[5-methyl-4-(4-pyridinyl)-1H-pyrazol-3  
60 yl]benzenamine;  
4-[3-(2,3-dihydrobenzofuran-5-yl)-5-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[3-(4-bromophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-(2-fluorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;  
65 4-[3-(3-fluorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-methyl-5-[3-(trifluoromethyl)phenyl]-1H-pyrazol-4  
yl]pyridine;  
4-(3-ethyl-4-phenyl-1H-pyrazol-4-yl)pyridine;  
4-[5-(3-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
70 4-[3-ethyl-5-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;  
4-[5-(3,4-difluorophenyl)-3-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[5-(3-ethoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-methyl-5-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-  
75 yl]pyridine;  
4-[3-methyl-5-(3-thienyl)-1H-pyrazol-4-yl]pyridine;  
4-[5-(2,4-dichlorophenyl)-3-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
80 4-[5-(3-chloro-4-methoxyphenyl)-3-methyl-1H-pyrazol-4-  
yl]pyridine;  
ethyl 3-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazole-5-  
propanoate;  
4-[3-(4-fluorophenyl)-1-methyl-pyrazol-4-yl]pyridine;  
85 5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-  
2-amine;  
5-[3-methyl-5-(3-methylphenyl)-1H-pyrazol-4-yl]pyrimidin-  
2-amine;



- 90 5-[3-methyl-5-(2-methylphenyl)-1H-pyrazol-4-yl]pyrimidin-2-amine;  
5-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-2-amine;  
5-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-2-amine;
- 95 5-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyrimidin-2-amine;  
5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-amine;  
4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-
- 100 amine;  
4-[5-(3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-amine;  
4-[5-(2-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-amine;
- 105 4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-amine;  
4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-amine;  
4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-
- 110 2-amine;  
5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-methoxypyridine;  
2-methoxy-5-[3-methyl-5-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;
- 115 2-methoxy-5-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-methoxypyridine;  
2-methoxy-4-[3-methyl-5-(3-methylphenyl)-1H-pyrazol-4-
- 120 yl]pyridine;  
2-methoxy-4-[3-methyl-5-(2-methylphenyl)-1H-pyrazol-4-yl]pyridine;  
4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-methoxypyridine;

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- 125 4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]-2-methoxypyridine;  
2-methoxy-4-[3-methyl-5-(4-methylphenyl)-1H-pyrazol-4-yl]pyridine;  
5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;  
130 4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;  
4-[5-(3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;  
135 4-[5-(2-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;  
4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;  
4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;  
140 4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridin-2-ol;  
5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;  
145 4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;  
4-[5-(3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;  
4-[5-(2-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;  
150 4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;  
4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;  
155 4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-methanamine;  
5-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;  
4-[5-(3-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;  
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- 4-[5-(3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;  
4-[5-(2-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;  
165 4-[5-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;  
4-[5-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;  
4-[5-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine-2-carboxamide;  
170 4-[5-(3-fluoro-4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(4-fluoro-3-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
175 4-[5-(4-chloro-3-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(2,3-dihydrobenzofuran-6-yl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(benzofuran-6-yl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
180 4-[5-(3-fluoro-5-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(3-chloro-5-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(1-cyclohexylen-1-yl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
185 4-[5-(1,3-cyclohexadien-1-yl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(5,6-dihydro-2H-pyran-4-yl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
190 4-(5-cyclohexyl-3-methyl-1H-pyrazol-4-yl)pyridine;  
4-[5-(4-methoxy-3-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(3-methoxy-4-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
195 4-[5-(3-methoxy-5-methylphenyl)-3-methyl-1H-pyrazol-4-yl]pyridine;

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- 4-[5-(3-furyl)-3-methyl-1H-pyrazol-4-yl]pyridine;  
2-methyl-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;  
2-methoxy-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;  
200 methyl 4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-2-carboxylate;  
4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-2-carboxamide;  
1-[4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridin-2-yl]ethanone;  
205 N,N-dimethyl-4-(3-methyl-5-phenyl-1H-pyrazol-2-yl)pyridin-2-amine;  
3-methyl-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;  
3-methoxy-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;  
210 methyl 4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-3-carboxylate;  
4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine-3-carboxamide;  
1-[4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridin-3-yl]ethanone;  
215 3-bromo-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyridine;  
N,N-dimethyl-4-(3-methyl-5-phenyl-1H-pyrazol-2-yl)pyridin-3-amine;  
2-methyl-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidine;  
220 4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidine;  
2-methoxy-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidine;  
4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine;  
N,N-dimethyl-4-(3-methyl-5-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine;  
225 4-(5,6-dihydro-2H-pyran-4-yl)-3-methyl-5-phenyl-1H-pyrazole;  
3-methyl-5-phenyl-4-(3-thienyl)-1H-pyrazole;  
4-(3-furyl)-3-methyl-5-phenyl-1H-pyrazole;  
230 3-methyl-5-phenyl-4-(2-thienyl)-1H-pyrazole;  
4-(2-furyl)-3-methyl-5-phenyl-1H-pyrazole;  
4-(3-isothiazolyl)-3-methyl-5-phenyl-1H-pyrazole

- 4-(3-isoxazolyl)-3-methyl-5-phenyl-1H-pyrazole;  
4-(5-isothiazolyl)-3-methyl-5-phenyl-1H-pyrazole;  
235 4-(5-isoxazolyl)-3-methyl-5-phenyl-1H-pyrazole;  
3-methyl-5-phenyl-4-(5-thiazolyl)-1H-pyrazole;  
3-methyl-4-(5-oxazolyl)-5-phenyl-1H-pyrazole;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;  
2-methyl-4-[3-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;  
240 4-(1-methyl-3-phenyl-1H-pyrazol-4-yl)pyridine;  
4-(3-phenyl-1H-pyrazol-4-yl)pyridine;  
2-methyl-4-(3-phenyl-1H-pyrazol-4-yl)pyridine;  
4-[3-(3-chlorophenyl)-1-methyl-pyrazol-4-yl]pyridine;  
4-[3-(4-chlorophenyl)-1-methyl-pyrazol-4-yl]pyridine;  
245 4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-2-methylpyridine;  
4-[3-(3-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-(3-fluorophenyl)-1H-pyrazol-4-yl]pyridine;  
250 4-[3-(3-chlorophenyl)-1-methyl-pyrazol-4-yl]-2-  
methylpyridine;  
5-(4-chlorophenyl)-N-phenyl-4-(4-pyridinyl)-1H-pyrazol-3-  
amine;  
5-(4-chlorophenyl)-N-methyl-4-(4-pyridinyl)-1H-pyrazol-3-  
255 amine;  
5-(4-chlorophenyl)-N,N-dimethyl-4-(4-pyridinyl)-1H-  
pyrazol-3-amine dihydrate;  
5-(3-fluorophenyl)-N,N-dimethyl-4-(4-pyridinyl)-1H-  
pyrazol-3-amine;  
260 N,N-dimethyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-  
pyrazol-3-amine;  
N-methyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-  
amine;  
N-ethyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-pyrazol-3-  
265 amine;  
N,N-diethyl-5-(3-methylphenyl)-4-(4-pyridinyl)-1H-  
pyrazol-3-amine;  
5-(4-chlorophenyl)-N,N-diethyl-4-(4-pyridinyl)-1H-

- pyrazol-3-amine;
- 270 4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]morpholine;
- 5-(4-chlorophenyl)-N-propyl-4-(4-pyridinyl)-1H-pyrazol-3-amine;
- 5-(4-chlorophenyl)-N-(phenylmethyl)-4-(4-pyridinyl)-1H-pyrazol-3-amine hydrate (2:1);
- 275 5-(4-chlorophenyl)-N-(2-methoxyethyl)-4-(4-pyridinyl)-1H-pyrazol-3-amine monohydrate;
- 1,1-dimethylethyl-4-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-piperazinecarboxylate;
- 280 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]piperazine trihydrochloride;
- 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine;
- 1,1-dimethylethyl 4-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-piperazinecarboxylate;
- 285 1-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]piperazine trihydrochloride;
- 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]piperazine;
- 290 N-[5-(4-chlorophenyl)-4-[2-(phenylmethyl)amino]-4-pyridinyl]-1H-pyrazol-3-yl]-1,3-propanediamine, trihydrochloride;
- 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-(phenylmethyl)piperazine;
- 295 4-[3-(4-fluorophenyl)-5-(1-piperazinyl)-1H-pyrazol-4-yl]pyrimidine, dihydrochloride;
- 1,1-dimethylethyl [3-[[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]amino]propyl]carbamate;
- N-[5-[4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,3-propanediamine, trihydrochloride monohydrate;
- 300 1,1-dimethylethyl [2-[[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]amino]ethyl]carbamate;
- 1,1-dimethylethyl 4-[5-(4-chlorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1-

- 305 piperazinecarboxylate;  
1,1-dimethylethyl 4-[5-(4-fluorophenyl)-4-(4-pyrimidinyl)-1H-pyrazol-3-yl]-1-piperazinecarboxylate;  
1,1-dimethylethyl [3-[[5-(4-chlorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-pyrazol-3-yl]amino]propyl]carbamate;  
310 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-ethylpiperazine;  
N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-1,2-ethanediamine;  
4-[3-(2,6-difluorophenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;  
315 4-[3-(3-ethylphenyl)-5-methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-(3-chlorophenyl)-5-ethyl-1H-pyrazol-4-yl]pyridine;  
4-[3-ethyl-5-(3-ethylphenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-chlorophenyl)-5-(1-methylethyl)-1H-pyrazol-4-yl]pyridine;  
320 4-[3-cyclopropyl-5-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-fluorophenyl)-5-(trifluoromethyl)-1H-pyrazol-4-yl]pyridine;  
325 4-[5-(cyclopropyl-3-(4-(fluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
5-cyclopropyl-3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol;  
3-(4-fluorophenyl)-5-(2-methoxy-4-pyridinyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol;  
330 4-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]-2(1H)-pyridinone;  
1-acetyl-4-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]-2(1H)-pyridinone;  
335 Ethyl 2-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]cyclopropanecarboxylate;  
2-[3-(4-fluorophenyl)-1-(2-hydroxyethyl)-4-(4-pyridinyl)-1H-pyrazol-5-yl]cyclopropanecarboxylic acid;  
3-(4-fluorophenyl)-5-(4-imidazolyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol;  
340

- 4-[3-(4-chloro-3-methylphenyl)-1H-pyrazol-4-yl]pyridine  
5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-3-  
carboxylic acid;  
5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-3-  
345 methanol;  
1-[[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-  
yl]carbonyl]piperazine;  
1,1-dimethylethyl 4-[[5-(4-fluorophenyl)-4-(4-pyridinyl)-  
1H-pyrazol-3-yl]carbonyl]-1-piperazinecarboxylate;  
350 4-(1,5-dimethyl-3-phenyl-1H-pyrazol-4-yl)pyridine;  
4-(1,3-dimethyl-5-phenyl-1H-pyrazol-4-yl)pyridine;  
4-[3-(4-chlorophenyl)-1,5-dimethyl-1H-pyrazol-4-  
yl]pyridine;  
4-[5-(4-chlorophenyl)-1,3-dimethyl-1H-pyrazol-4-  
355 yl]pyridine;  
4-[5-ethyl-1-methyl-3-(3-methylphenyl)-1H-pyrazol-4-  
yl]pyridine;  
4-[3-ethyl-1-methyl-5-(3-methylphenyl)-1H-pyrazol-4-  
yl]pyridine;  
360 4-[3-(4-chlorophenyl)-1-ethyl-5-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[3-(4-chlorophenyl)-2-ethyl-5-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;  
365 4-[3-(2-chlorophenyl)-1H-pyrazol-4-yl]pyridine;  
3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol;  
3-(4-fluorophenyl)-4-(4-pyrimidinyl)-1H-pyrazole-1-  
ethanol;  
4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
370 2-[[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-  
pyridinyl]amino]-1-butanol;  
4-[5-bromo-3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-  
yl]pyridine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-  
375 pyridinecarbonitrile;  
4-[2-[3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-1-



- yl]ethyl]morpholine;  
3-(4-fluorophenyl)-1-methyl- $\alpha$ -phenyl-4-(4-pyridinyl)-1H-pyrazole-5-methanol;  
380 N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-morpholineethanamine;  
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-2(1H)-pyridinone hydrazone;  
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-N-(phenylmethyl)-  
385 2-pyridinamine;  
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-N-(phenylethyl)-2-pyridinamine;  
4-[3-(3-chlorophenyl)-1H-pyrazol-4-yl]-N-ethyl-2-pyridinamine;  
390 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinecarboxamide;  
Methyl 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinecarboxylate;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-methyl-2-pyridinecarboxamide;  
395 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinecarboxylic acid;  
4-[3-(3-fluorophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(1,3-benzodioxol-5-yl)-1H-pyrazol-4-yl]pyridine;  
400 4-[3-(3-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(1,3-benzodioxol-5-y)-1-methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
405 4-[3-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-methylpyridine;  
4-[5-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-methylpyridine;  
4-[3-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
4-[5-(3-chlorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
410 2-methyl-4-[1-methyl-3-(3-methylphenyl)-1H-pyrazol-4-yl]pyridine;  
2-methyl-4-[1-methyl-5-(3-methylphenyl)-1H-pyrazol-4

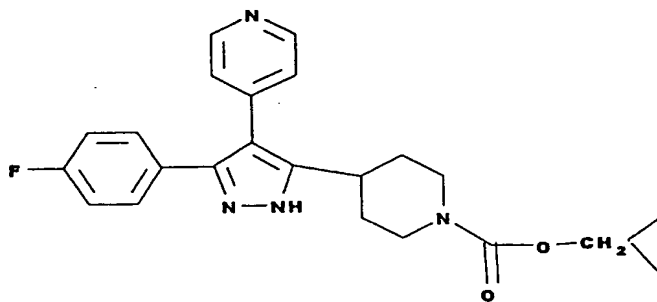
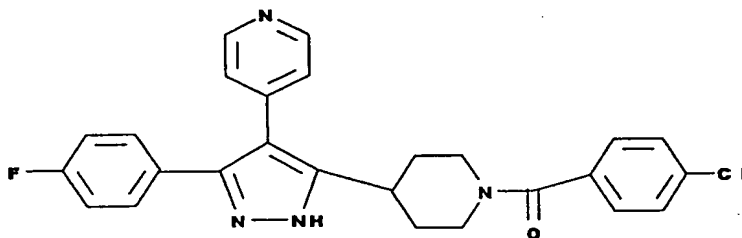
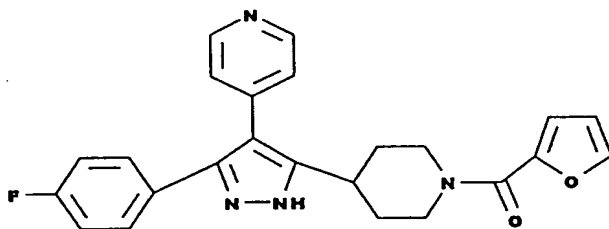
- yl]pyridine;  
4-(3-phenyl-1H-pyrazol-4-yl)pyridine;  
415 4-[3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]pyridine  
;  
4-[1-methyl-3-[3-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl  
]pyridine;  
4-[3-(3,4-difluorophenyl)-1H-pyrazol-4-yl]pyridine;  
420 4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-2-fluoropyridine;  
4-[3-(4-bromophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(3,4-difluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridi  
ne;  
4-[3-(4-bromophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
425 (E)-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-(2-phenyleth  
enyl)pyridine;  
(S)-4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-N-(2-methylbut  
yl)-2-pyridinamine;  
4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-N-[(4-methoxy-  
430 phenyl)methyl]-2-pyridinamine;  
N-[4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-  
2-pyridinemethanamine;  
N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-  
2-pyridinemethanamine;  
435 2-fluoro-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-iodophenyl)-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-iodophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine;  
4-[1-methyl-3-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl  
]pyridine;  
440 N-[1-(4-fluorophenyl)ethyl]-4-[3-(4-fluorophenyl)-1H-pyra  
zol-4-yl]-2-pyridinamine;  
N-[(3-fluorophenyl)methyl]-4-[3-(4-fluorophenyl)-1H-pyraz  
ol-4-yl]-2-pyridinamine;  
4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-(1-  
445 methylhydrazino)pyridine;  
2-fluoro-4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]p  
yridine;  
4-[3-(3,4-difluorophenyl)-1H-pyrazol-4-yl]-2-fluoro-

- pyridine;
- 450 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-3-methylpyridine;  
4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-3-methyl-  
pyridine;  
4-[3-(3,4-difluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-flu-  
oropyridine;
- 455 3-(4-fluorophenyl)-N,N-dimethyl-4-(4-pyridinyl)-1H-pyrazo-  
le-1-ethanamine;  
2-[2-(4-fluorophenyl)ethyl]-4-[3-(4-fluorophenyl)-1-  
methyl-1H-pyrazol-4-yl]pyridine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-[1-
- 460 (phenylmethyl)-4-piperidinyl]-2-pyridinamine;  
N'-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-  
N,N-dimethyl-1,2-ethanediamine;  
2,4-bis[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine;  
N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]-4-
- 465 morpholineethanamine;  
3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-pyrazole-  
1-ethanol;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-[2-(1H-imidazol-  
1-yl)ethyl]-2-pyridinamine;
- 470 4-[2-[3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-  
pyrazol-1-yl]ethyl]morpholine;  
(E)-3-(4-fluorophenyl)-4-[2-[2-(4-fluorophenyl)ethenyl]-  
4-pyridinyl]-1H-pyrazole-1-ethanol;  
3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-N,N-dimethyl-
- 475 1H-pyrazole-1-ethanamine;  
3-(4-fluorophenyl)-4-[2-[2-(4-fluorophenyl)ethyl]-4-  
pyridinyl]-1H-pyrazole-1-ethanol;  
4-[1-[2-(dimethylamino)ethyl]-3-(4-fluorophenyl)-1H-  
pyrazol-4-yl]-N,N-dimethyl-2-pyridinamine;
- 480 4-[1-[2-(dimethylamino)ethyl]-3-(4-fluorophenyl)-1H-  
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3-(4-fluorophenyl)-4-[2-[2-(4-fluorophenyl)ethyl]-4-  
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N-[(4-fluorophenyl)methyl]-4-[3(or 5)-(4-fluorophenyl)-1-

- 485 [[2-(4-morpholinyl)ethyl]-1H-pyrazol-4-yl]-2-pyridinamine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-4-piperadinyl-2-pyridinamine;  
N,N-diethyl-3-(4-fluorophenyl)-4-(2-fluoro-4-pyridinyl)-1H-pyrazole-1-ethanamine;  
490 4-[1-[2-(diethylamino)ethyl]-3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-[(4-fluorophenyl)methyl]-2-pyridinamine;  
2-[[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]amino]ethanol;  
495 2-[[4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-pyridinyl]amino]ethanol;  
3-[[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyridinyl]amino]-1-propanol;  
3-(4-fluorophenyl)-4-[2-[[4-(4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;  
500 5-(4-fluorophenyl)-4-[2-[[4-(4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;  
N,N-diethyl-3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanamine;  
505 N-[(4-fluorophenyl)methyl]-4-[3-(4-fluorophenyl)-1-[2-(4-morpholinyl)ethyl]-1H-pyrazol-4-yl]-2-pyridinamine;  
N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-morpholinepropanamine;  
N'-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-  
510 N,N-dimethyl-1,3-propanediamine;  
5-(4-fluorophenyl)-N-2-propynyl-4-(4-pyridinyl)-1H-pyrazol-3-amine;  
3-(4-fluorophenyl)-4-[2-[[4-(4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;  
515 5-(4-fluorophenyl)-4-[2-[[4-(4-fluorophenyl)methyl]amino]-4-pyridinyl]-1H-pyrazole-1-ethanol;  
4-[3-[(4-fluorophenyl)-1H-pyrazol-4-yl]quinoline;  
N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]glycine methyl ester;  
520 N-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-

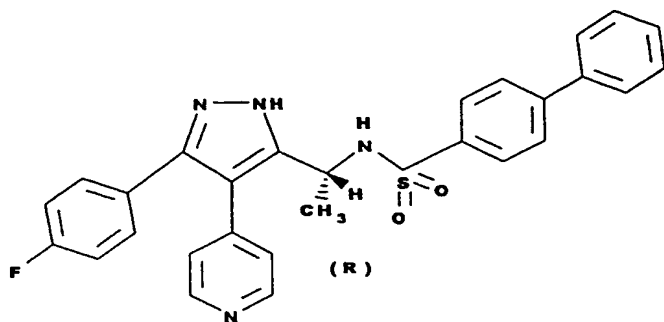
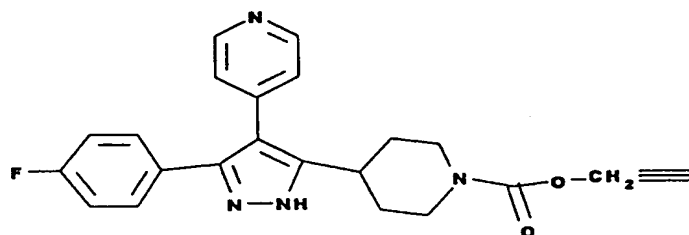
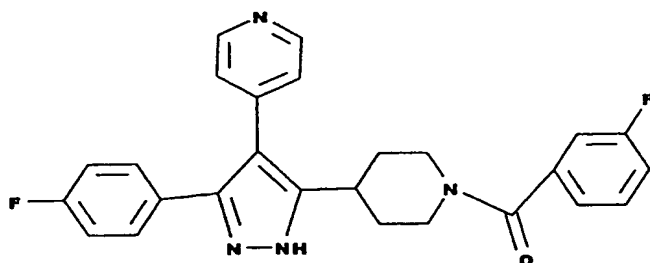
- yl]glycine;  
4-[3-(4-fluorophenyl)-1-(2-propynyl)-1H-pyrazol-4-yl]pyridine;  
4-[5-(4-fluorophenyl)-1-(2-propynyl)-1H-pyrazol-4-yl]pyridine;  
525 4,4'-(1H-pyrazole-3,4-diyl)bis[pyridine];  
4-[3-(3,4-dichlorophenyl)-1H-pyrazol-4-yl]pyridine;  
N-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-piperidinamine;  
530 2-Chloro-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyrimidine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2(1H)-pyrimidinone hydrazone;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N,N-dimethyl-2-pyrimidinamine;  
535 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-methyl-2-pyrimidinamine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-(phenylmethyl)-2-pyrimidinamine;  
540 N-cyclopropyl-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinamine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-N-[(4-methoxyphenyl)methyl]-2-pyrimidinamine;  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinamine;  
545 N-[4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]-N-(phenylmethyl)acetamide;  
Ethyl [4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-2-pyrimidinyl]carbamate;  
4-[3-(3-methylphenyl)-1H-pyrazol-4-yl]pyrimidine;  
550 4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]pyrimidine;  
4-[3-(3-fluorophenyl)-1H-pyrazol-4-yl]pyrimidine; and  
4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyrimidine.

70. A compound of Claim 1 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of



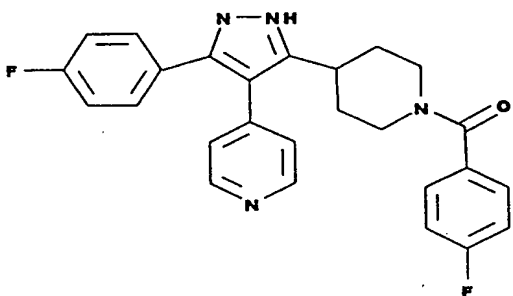
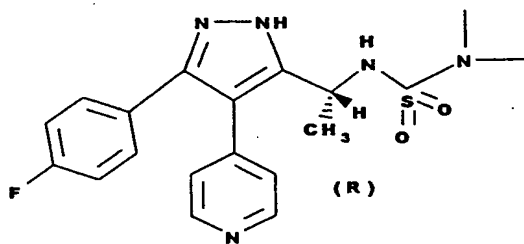
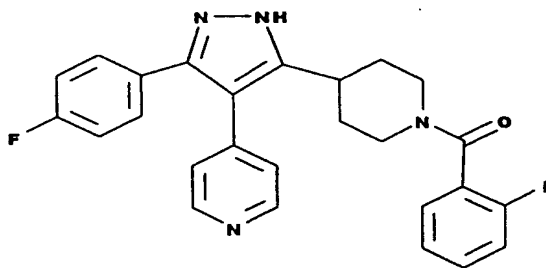
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SUBSTITUTESHEET (RULE 26)

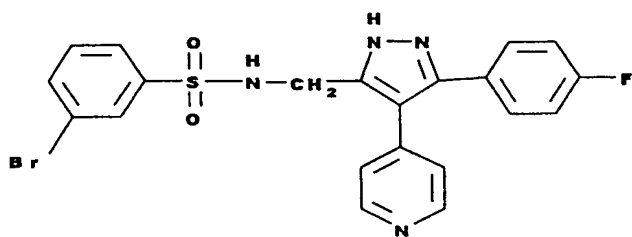
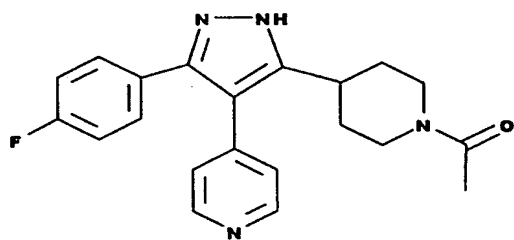
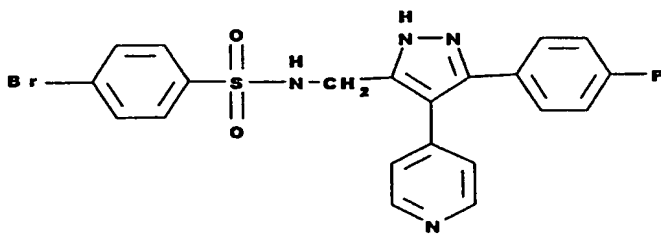
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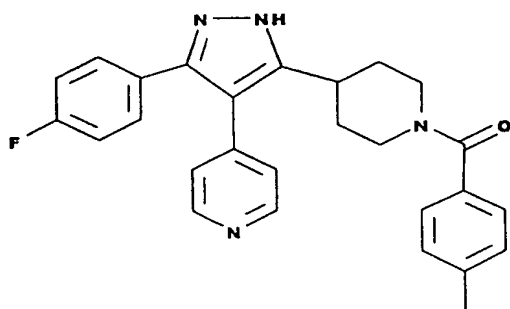
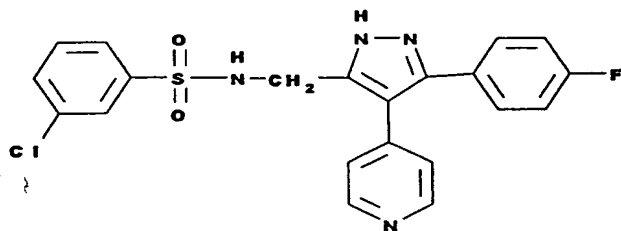
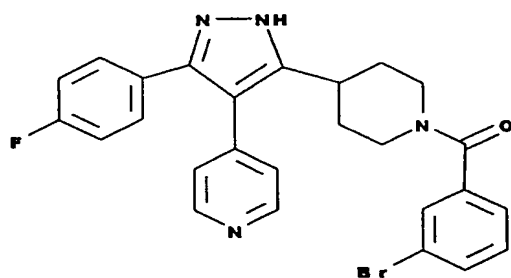


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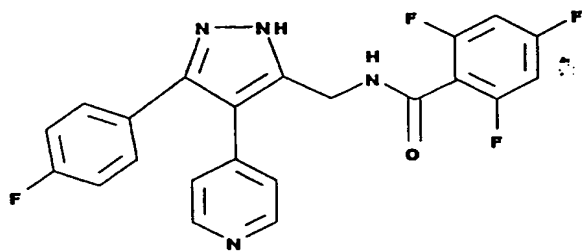
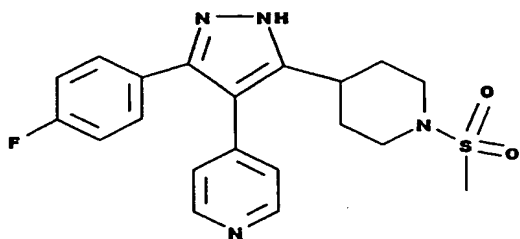
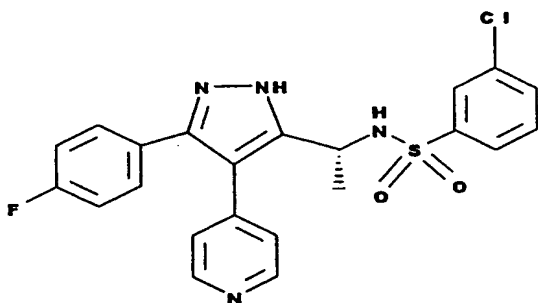
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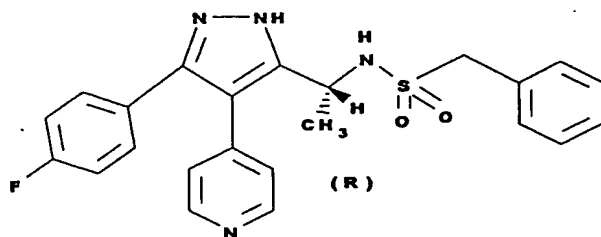
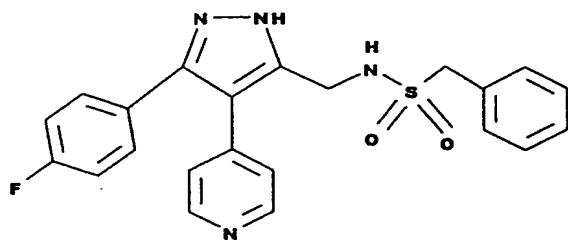
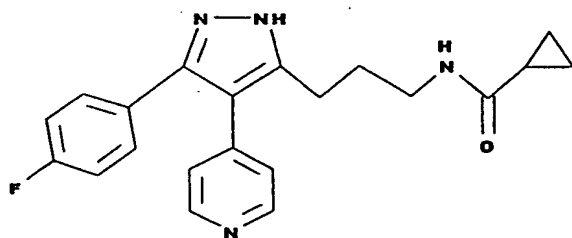
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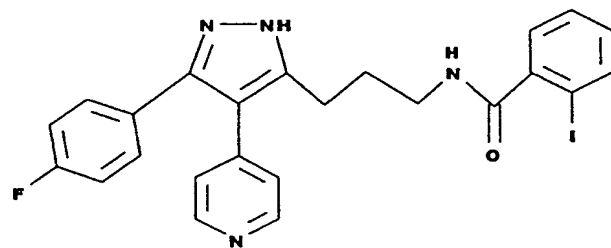
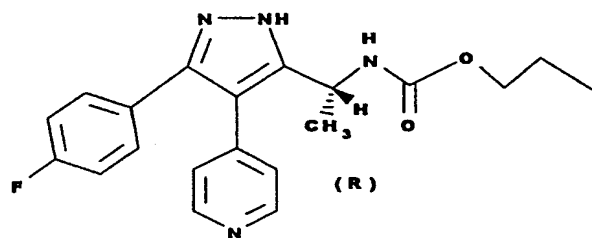
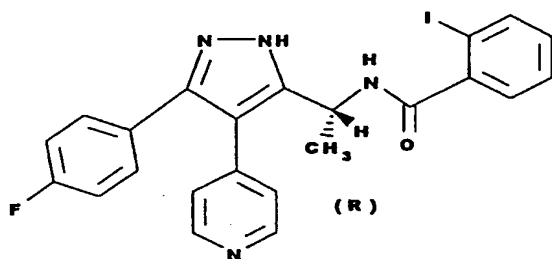
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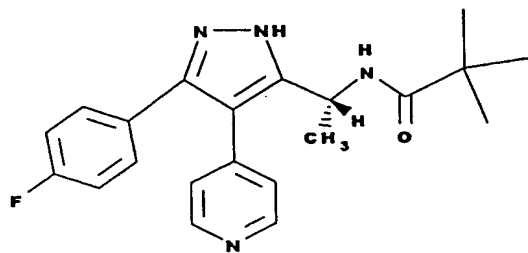
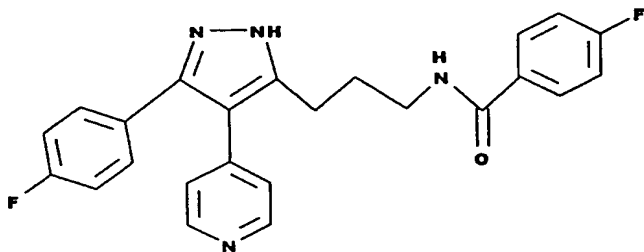
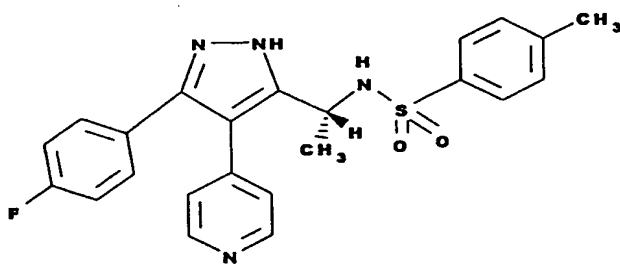


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71. A compound of claim 1 that is 4-[5-(4-fluorophenyl)-1-(2-propynyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

72. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1-(2-propynyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

73. A compound of claim 1 that is 3-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrazole-1-ethanol or a pharmaceutically-acceptable salt or a tautomer thereof.

74. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]-2-(1-methylhydrazino)pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

75. A compound of claim 1 that is 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]piperazine or a pharmaceutically-acceptable salt or a tautomer thereof.

76. A compound of claim 1 that is 4-[3-cyclopropyl-5-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

77. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

78. A compound of claim 1 that is 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine or a pharmaceutically-acceptable salt or a tautomer thereof.

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79. A compound of claim 1 that is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyrimidine or a pharmaceutically-acceptable salt or a tautomer thereof.

80. A compound of claim 1 that is 2-fluoro-4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

81. A compound of claim 1 that is 4-[3-(3,4-difluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

82. A compound of claim 1 that is 4-[3-(4-bromophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

83. A compound of claim 1 that is 4-[3-(4-chlorophenyl)-1H-pyrazol-4-yl]-2-fluoropyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

84. A compound of claim 1 that is 4-[3-(1,3-benzodioxol-5-yl)-1-methyl-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

85. A compound of claim 1 that is 4-[3-(3-fluorophenyl)-1-methyl-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

86. A compound of claim 1 that is 4-[3-(3-fluorophenyl)-1-methyl-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

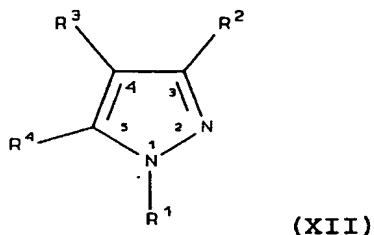


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87. A compound of claim 1 that is 5-(4-fluorophenyl)-N-2-propynyl-4-(4-pyridinyl)-1H-pyrazol-3-amine or a pharmaceutically-acceptable salt or a tautomer thereof.

88. A substituted pyrazole that specifically binds to an ATP binding site of p38 kinase.

89. A compound of claim 88 having the formula:



wherein

5 R<sup>1</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units; and

R<sup>2</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical that binds with p38 kinase at said ATP binding site of p38 kinase; and

10 R<sup>3</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a hydrogen bond acceptor functionality; and

15 R<sup>4</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units;

provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl ring containing a 2-hydroxy substituent and when R<sup>1</sup> is hydrido; further provided R<sup>2</sup> is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl  
20 when R<sup>4</sup> is hydrido; and further provided R<sup>4</sup> is not

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methanesulfonylphenyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

90. A compound of claim 89 wherein R<sup>2</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical that binds with Lys<sub>52</sub>, Glu<sub>69</sub>, Leu<sub>73</sub>, Ile<sub>82</sub>, Leu<sub>84</sub>, Leu<sub>101</sub>, and Thr<sub>103</sub> sidechains at said ATP binding site of p38 kinase, said radical being substantially disposed within a hydrophobic cavity formed during said binding by p38 kinase at the ATP binding site.

91. A compound of claim 89 wherein R<sup>3</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a hydrogen bond acceptor functionality that hydrogen bonds with the N-H backbone of Met<sub>106</sub> of p38 kinase.

92. A compound of claim 89 wherein R<sup>1</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 250 atomic mass units.

93. A compound of claim 89 wherein R<sup>4</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 250 atomic mass units.

94. A compound of claim 89 wherein R<sup>1</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units; and R<sup>2</sup> is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical wherein said radical binds with Lys<sub>52</sub>, Glu<sub>69</sub>, Leu<sub>73</sub>, Ile<sub>82</sub>, Leu<sub>84</sub>, Leu<sub>101</sub>, and Thr<sub>103</sub> sidechains

at said ATP binding site of p38 kinase, said radical being substantially disposed within a hydrophobic cavity formed during said binding by p38 kinase at the ATP binding site; and

10  $R^3$  is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a hydrogen bond acceptor functionality that hydrogen bonds with the N-H backbone of Met<sub>106</sub> of p38 kinase; and

15  $R^4$  is a hydrocarbyl, heterosubstituted hydrocarbyl or heterocyclyl radical having a molecular weight less than about 360 atomic mass units.

95. A compound of claim 94 wherein  $R^1$  and  $R^4$  are independently selected from hydrocarbyl, heterosubstituted hydrocarbyl and heterocyclyl radicals and have a combined molecular weight less than about 360 atomic mass units.

96. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claims 1; or a pharmaceutically acceptable salt thereof.

97. A pharmaceutical composition of Claim 96 wherein said compound is selected from the compounds of Claim 3; or a pharmaceutically acceptable salt thereof.

98. A pharmaceutical composition of Claim 96 wherein said compound is selected from the compounds of Claim 4; or a pharmaceutically acceptable salt thereof.

99. A pharmaceutical composition of Claim 96 wherein said compound is selected from the compounds of Claim 5; or a pharmaceutically acceptable salt thereof.

100. A pharmaceutical composition of Claim 96

wherein said compound is selected from the compounds of Claim 6; or a pharmaceutically acceptable salt thereof.

101. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 24; or a pharmaceutically acceptable salt thereof.

102. A pharmaceutical composition of Claim 101 wherein said compound is selected from the compounds of Claim 25; or a pharmaceutically acceptable salt thereof.

103. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 25; or a pharmaceutically acceptable salt thereof.

104. A pharmaceutical composition of Claim 103 wherein said compound is selected from the compounds of Claim 36; or a pharmaceutically acceptable salt thereof.

105. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 44; or a pharmaceutically acceptable salt thereof.

106. A pharmaceutical composition of Claim 105 wherein said compound is selected from the compounds of Claim 45; or a pharmaceutically acceptable salt thereof.

107. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claim 53; or a pharmaceutically acceptable salt thereof.

108. A pharmaceutical composition of Claim 107

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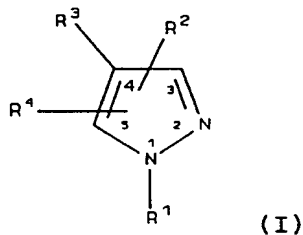
wherein said compound is selected from the compounds of Claim 54; or a pharmaceutically acceptable salt thereof.

109. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the of compounds of Claim 66; or a pharmaceutically acceptable salt thereof.

110. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from the compounds of Claims 69; or a pharmaceutically salt thereof.

111. A pharmaceutical composition of Claim 110 wherein said compound is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

112. A method of treating a TNF mediated disorder, said method comprising treating the subject having or susceptible to such disorder with a therapeutically-effective amount of a compound of Formula I



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wherein

R<sup>1</sup> is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl,

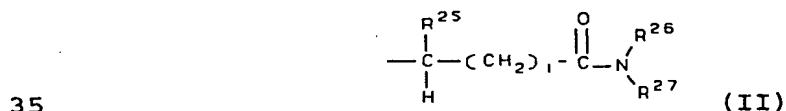
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haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
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 30 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



wherein:

$i$  is an integer from 0 to 9;

$R^{25}$  is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 40 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 heterocyclylcarbonylaminoalkylene; and

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R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxycarbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene, alkoxycarbonylalkoxylarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene, aralkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, arylsulfonylaminoalkylene, alkylsulfonylarylene, alkylaminosulfonylarylene; wherein said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylheterocyclylarylene, alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene, aryloxycarbonylarylene, arylcarbonylarylene, alkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, and alkylsulfonylarylene groups are optionally substituted with one or more radicals independently selected from alkyl, halo, haloalkyl,

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- alkoxy, keto, amino, nitro, and cyano; or
- 80  $R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$  is selected from aralkyl, aralkoxyalkylene, heterocyclylalkylene, alkylheterocyclylalkylene, alkoxycarbonylalkylene, alkylthioalkylene, and aralkylthioalkylene; wherein said aralkyl and
- 85 heterocyclyl groups are optionally substituted with one or more radicals independently selected from alkyl and nitro; or
- $R^{26}$  and  $R^{27}$  together with the nitrogen atom to which they are attached form a heterocycle, wherein said
- 90 heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocyclyl, heterocyclylalkylene, alkylheterocyclylalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
- 95 alkoxycarbonylamino; wherein said aryl, heterocyclylalkylene and aryloxyalkylene radicals are optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy;
- 100 and
- $R^2$  is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, alkylamino, alkenylamino, alkynylamino, arylamino,
- 105 heterocyclylamino, heterocyclylalkylamino, aralkylamino, aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocycliloxy, alkylthio,
- 110 arylthio, heterocyclylthio, carboxy, carboxyalkyl, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,

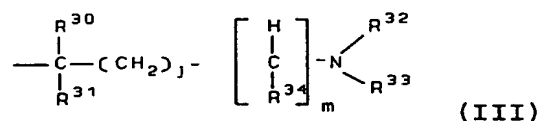
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- 115 alkoxy-carbonylaminoalkylamino, and heterocyclisulfonyl;  
 wherein the aryl, heterocyclyl, heterocyclalkyl,  
 cycloalkyl and cycloalkenyl groups are optionally  
 substituted with one or more radicals independently  
 selected from halo, keto, amino, alkyl, alkenyl, alkynyl,  
 120 aryl, heterocyclyl, aralkyl, heterocyclalkyl,  
 epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy,  
 aralkoxy, haloalkyl, alkylamino, alkynylamino,  
 alkylaminoalkylamino, heterocyclalkylamino,  
 alkylcarbonyl, alkoxy-carbonyl, alkylsulfonyl,  
 125 arylsulfonyl, and aralkylsulfonyl; or

$R^2$  has the formula:



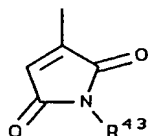
wherein:

- j is an integer from 0 to 8; and  
 130 m is 0 or 1; and  
 $R^{30}$  and  $R^{31}$  are independently selected from hydrogen,  
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclalkylene,  
 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,  
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and  
 135  $R^{32}$  is selected from hydrogen, alkyl, aralkyl,  
 heterocyclalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 heterocyclalkylcarbonylaminoalkylene;  
 140  $R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  
 $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ , wherein  $R^{35}$ ,  
 $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently selected from  
 hydrocarbon, heterosubstituted hydrocarbon and  
 heterocyclyl; and  
 145  $R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl,  
 alkylaminocarbonyl, and arylaminocarbonyl; or

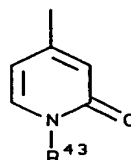
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$R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and  
 $R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl,



; and



150

(IV)

(V)

wherein  $R^{43}$  is selected from hydrogen, alkyl,  
 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;  
 and

155 wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl and  
 purinyl groups are optionally substituted with one or  
 more radicals independently selected from halo, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 160 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 alkenylamino, alkynylamino, cycloalkylamino,  
 cycloalkenylamino, arylamino, heterocyclylamino,  
 aminocarbonyl, cyano, hydroxy, hydroxyalkyl,  
 165 alkoxycarbonyl, aryloxcarbonyl, heterocyclylloxycarbonyl,  
 alkoxycarbonylamino, alkoxyaralkylamino, aminosulfinyl,  
 aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino,  
 aralkylamino, heterocyclylalkylamino,  
 aralkylheterocyclylamino, nitro, alkylaminocarbonyl,  
 170 alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl,  
 alkylcarbonyl, hydrazinyl, alkylhydrazinyl,  
 arylhydrazinyl, or  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or  
 amino, and  $R^{45}$  is alkyl or aralkyl; and

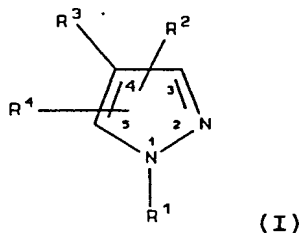
175  $R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,  
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 $R^4$  is optionally substituted with one or more radicals

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independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene, alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene, arylaminoalkylene, aminoalkylamino, and hydroxy; provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl ring containing a 2-hydroxy substituent and when R<sup>1</sup> is hydrido; further provided R<sup>2</sup> is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R<sup>4</sup> is hydrido; and further provided R<sup>4</sup> is not methylsulfonylphenyl; or a pharmaceutically-acceptable salt or tautomer thereof.

113. A method of treating a p38 kinase mediated disorder, said method comprising treating the subject having or susceptible to such disorder with a therapeutically-effective amount of a compound of Formula I

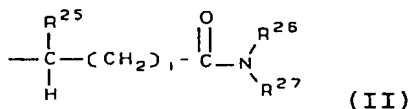


wherein

R<sup>1</sup> is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl,

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- 10 cycloalkylalkylene, cycloalkenylalkylene,  
heterocyclylalkylene, haloalkyl, haloalkenyl,  
haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,  
arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,  
15 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl,  
heterocyclioxyalkyl, alkoxyalkoxy, mercaptoalkyl,  
alkylthioalkylene, alkenylthioalkylene,  
alkylthioalkenylene, amino, aminoalkyl, alkylamino,  
alkenylamino, alkynylamino, arylamino, heterocyclylamino,  
20 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,  
arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,  
alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
heterocyclylsulfonyl, alkylaminoalkylene,  
alkylsulfonylalkylene, acyl, acyloxycarbonyl,  
25 alkoxycarbonylalkylene, aryloxycarbonylalkylene,  
heterocyclioxycarbonylalkylene, alkoxycarbonylarylene,  
aryloxycarbonylarylene, heterocyclioxycarbonylarylene,  
alkylcarbonylalkylene, arylcarbonylalkylene,  
heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
30 arylcarbonylarylene, heterocyclylcarbonylarylene,  
alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
arylcarbonyloxyarylene, and  
heterocyclylcarbonyloxyarylene; or  
35  $R^1$  has the formula .



wherein:

- $i$  is an integer from 0 to 9;  
 $R^{25}$  is selected from hydrogen, alkyl, aralkyl,  
40 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
aminoalkyl, alkylaminoalkyl, arylaminoalkyl,

alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene; and

45  $R^{26}$  is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

$R^{27}$  is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, 50 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, 55 aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, 60 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxycarbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, 65 alkoxycarbonylheterocyclylarylene, alkoxycarbonylalkoxyarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene, aralkylthioarylene, heterocyclylthioarylene, 70 arylthioalkylarylene, arylsulfonylaminoalkylene, alkylsulfonylarylene, alkylaminosulfonylarylene; wherein said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylheterocyclylarylene, alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene, 75 aryloxycarbonylarylene, arylcarbonylarylene, alkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, and alkylsulfonylarylene groups

are optionally substituted with one or more radicals independently selected from alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano; or

80  $R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$  is selected from aralkyl, aralkoxyalkylene, heterocyclalkylene, alkylheterocyclalkylene, alkoxycarbonylalkylene, alkylthioalkylene, and  
85 aralkylthioalkylene; wherein said aralkyl and heterocycl groups are optionally substituted with one or more radicals independently selected from alkyl and nitro; or

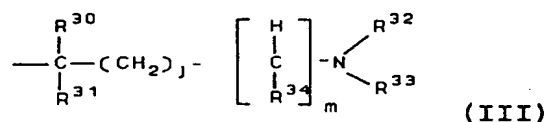
$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
90 they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocycl, heterocyclalkylene, alkylheterocyclalkylene, aryloxyalkylene,  
95 alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and alkoxycarbonylamino; wherein said aryl, heterocyclalkylene and aryloxyalkylene radicals are optionally substituted with one or more radicals  
100 independently selected from halogen, alkyl and alkoxy; and

$R^2$  is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocycl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocycl, heterocyclalkyl,  
105 alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclamino, heterocyclalkylamino, aralkylamino, aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl,  
110 cycloalkenyl, alkoxy, heterocyclloxy, alkylthio, arylthio, heterocyclthio, carboxy, carboxyalkyl, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclcarbonyl,

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- alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl,  
 115 alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
 alkoxycarbonylaminoalkylamino, and heterocyclylsulfonyl;  
 wherein the aryl, heterocyclyl, heterocyclylalkyl,  
 cycloalkyl and cycloalkenyl groups are optionally  
 substituted with one or more radicals independently  
 120 selected from halo, keto, amino, alkyl, alkenyl, alkynyl,  
 aryl, heterocyclyl, aralkyl, heterocyclylalkyl,  
 epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy,  
 aralkoxy, haloalkyl, alkylamino, alkynylamino,  
 alkylaminoalkylamino, heterocyclylalkylamino,  
 125 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,  
 arylsulfonyl, and aralkylsulfonyl; or

R<sup>2</sup> has the formula:



wherein:

- 130 j is an integer from 0 to 8; and  
 m is 0 or 1; and  
 R<sup>30</sup> and R<sup>31</sup> are independently selected from hydrogen,  
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,  
 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,  
 135 alkoxyalkyl, and alkylcarbonyloxyalkyl; and  
 R<sup>32</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 140 heterocyclylcarbonylaminoalkylene;  
 R<sup>33</sup> is selected from hydrogen, alkyl, -C(O)R<sup>35</sup>,  
 -C(O)OR<sup>35</sup>, -SO<sub>2</sub>R<sup>36</sup>, -C(O)NR<sup>37</sup>R<sup>38</sup>, and -SO<sub>2</sub>NR<sup>39</sup>R<sup>40</sup>, wherein R<sup>35</sup>,  
 R<sup>36</sup>, R<sup>37</sup>, R<sup>38</sup>, R<sup>39</sup> and R<sup>40</sup> are independently selected from  
 hydrocarbon, heterosubstituted hydrocarbon and  
 145 heterocyclyl; and

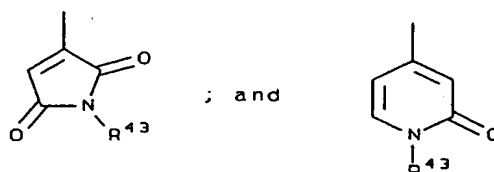
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$R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

$R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and

$R^3$  is selected from pyridinyl, pyrimidinyl,  
150 quinolinyl, purinyl,



(IV)

(V)

wherein  $R^{43}$  is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;  
155 and

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
160 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, heterocyclylamino,  
165 aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxy carbonyl, aryloxy carbonyl, heterocyclylalkoxy carbonyl, alkoxy carbonylamino, alkoxy aralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, heterocyclylalkylamino,  
170 aralkylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, or  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and

175  $R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,

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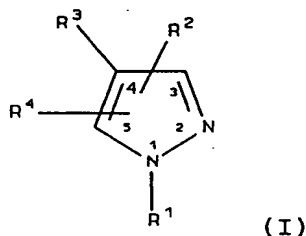


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cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R<sup>4</sup> is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene, alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene, arylaminoalkylene, aminoalkylamino, and hydroxy; provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl ring containing a 2-hydroxy substituent and when R<sup>1</sup> is hydrido; further provided R<sup>2</sup> is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R<sup>4</sup> is hydrido; and further provided R<sup>4</sup> is not methylsulfonylphenyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

114. A method of treating inflammation, said method comprising treating the subject having or susceptible to inflammation with a therapeutically-effective amount of a compound of Formula I



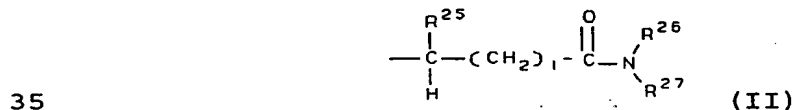
wherein

R<sup>1</sup> is selected from hydrido, alkyl, cycloalkyl,

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- alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
- 10 heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl,
- 15 heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
- 20 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene,
- 25 heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene,
- 30 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,

- 40 aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene; and
- R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, 45 alkoxycarbonylalkylene, and alkylaminoalkyl; and
- R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, 50 alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, 55 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, 60 arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxy carbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene, 65 alkoxycarbonylalkoxyarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene, aralkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, arylsulfonylaminoalkylene, 70 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylheterocyclylarylene, alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene, aryloxycarbonylarylene, arylcarbonylarylene, 75 alkylthioarylene, heterocyclylthioarylene,

arylthioalkylarylene, and alkylsulfonylarylene groups are optionally substituted with one or more radicals independently selected from alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano; or

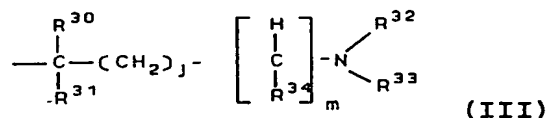
80  $R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$  is selected from aralkyl, aralkoxyalkylene, heterocyclalkylene, alkylheterocyclalkylene, alkoxycarbonylalkylene, alkylthioalkylene, and aralkylthioalkylene; wherein said aralkyl and  
85 heterocycl groups are optionally substituted with one or more radicals independently selected from alkyl and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which they are attached form a heterocycle, wherein said  
90 heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocycl, heterocyclalkylene, alkylheterocyclalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
95 alkoxycarbonylamino; wherein said aryl, heterocyclalkylene and aryloxyalkylene radicals are optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy;  
100 and

$R^2$  is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocycl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocycl, heterocyclalkyl, alkylamino, alkenylamino, alkynylamino, arylamino,  
105 heterocyclamino, heterocyclalkylamino, aralkylamino, aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocyclloxy, alkylthio,  
110 arylthio, heterocyclthio, carboxy, carboxyalkyl, carboxycycloalkyl, carboxycycloalkenyl,

carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino, 115 alkoxycarbonylaminoalkylamino, and heterocyclylsulfonyl; wherein the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and cycloalkenyl groups are optionally substituted with one or more radicals independently selected from halo, keto, amino, alkyl, alkenyl, alkynyl, 120 aryl, heterocyclyl, aralkyl, heterocyclylalkyl, epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclylalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, 125 arylsulfonyl, and aralkylsulfonyl; or

R<sup>2</sup> has the formula:



wherein:

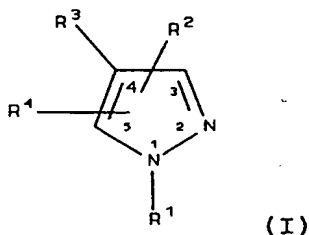
- j is an integer from 0 to 8; and  
 130 m is 0 or 1; and  
 R<sup>30</sup> and R<sup>31</sup> are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and  
 135 R<sup>32</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;  
 140 R<sup>33</sup> is selected from hydrogen, alkyl, -C(O)R<sup>35</sup>, -C(O)OR<sup>35</sup>, -SO<sub>2</sub>R<sup>36</sup>, -C(O)NR<sup>37</sup>R<sup>38</sup>, and -SO<sub>2</sub>NR<sup>39</sup>R<sup>40</sup>, wherein R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup>, R<sup>38</sup>, R<sup>39</sup> and R<sup>40</sup> are independently selected from hydrocarbon, heterosubstituted hydrocarbon and



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R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl,  
 175 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 R<sup>4</sup> is optionally substituted with one or more radicals  
 independently selected from halo, alkyl, alkenyl,  
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
 180 alkylsulfinylalkylene, arylsulfinylalkylene,  
 alkylsulfonyl, alkylsulfonylalkylene,  
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
 185 nitro, alkylamino, arylamino, alkylaminoalkylene,  
 arylaminoalkylene, aminoalkylamino, and hydroxy;  
 provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl ring  
 containing a 2-hydroxy substituent and when R<sup>1</sup> is hydrido;  
 further provided R<sup>2</sup> is selected from aryl, heterocyclyl,  
 190 unsubstituted cycloalkyl and cycloalkenyl when R<sup>4</sup> is  
 hydrido; and further provided R<sup>4</sup> is not  
 methylsulfonylphenyl; or  
 a pharmaceutically-acceptable salt or tautomer  
 thereof.

115. A method of treating arthritis, said method  
 comprising treating the subject having or susceptible to  
 arthritis with a therapeutically-effective amount of a  
 compound of Formula I



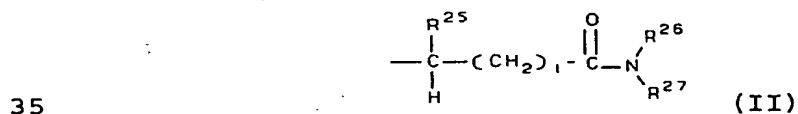
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wherein

$R^1$  is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



wherein:

$i$  is an integer from 0 to 9;



R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene; and

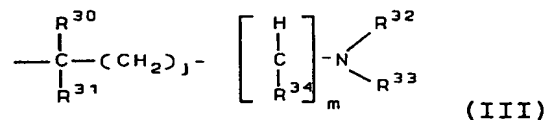
R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxycarbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene, alkoxycarbonylalkoxylarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene, aralkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, arylsulfonylaminoalkylene, alkylsulfonylarylene, alkylaminosulfonylarylene; wherein said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylheterocyclylarylene, alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,

- aryloxycarbonylarylene, arylcarbonylarylene,  
75 alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
are optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
80  $R^{27}$  is  $-\text{CHR}^{28}\text{R}^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
85 heterocyclyl groups are optionally substituted with one  
or more radicals independently selected from alkyl and  
nitro; or  
 $R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
90 heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
95 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
heterocyclylalkylene and aryloxyalkylene radicals are  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
100 and  
 $R^2$  is selected from hydrido, halogen, alkyl, alkenyl,  
alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl,  
aralkyl, alkylheterocyclyl, heterocyclylalkyl,  
alkylamino, alkenylamino, alkynylamino, arylamino,  
105 heterocyclylamino, heterocyclylalkylamino, aralkylamino,  
aminoalkyl, aminoaryl, aminoalkylamino,  
arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,  
alkylaminoarylene, alkylaminoalkylamino, cycloalkyl,  
cycloalkenyl, alkoxy, heterocyclyoxy, alkylthio,

- 110 arylthio, heterocyclylthio, carboxy, carboxyalkyl, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonyl, alkoxylalkylamino, 115 alkoxycarbonylaminoalkylamino, and heterocyclylsulfonyl; wherein the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and cycloalkenyl groups are optionally substituted with one or more radicals independently selected from halo, keto, amino, alkyl, alkenyl, alkynyl, 120 aryl, heterocyclyl, aralkyl, heterocyclylalkyl, epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclylalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, 125 arylsulfonyl, and aralkylsulfonyl; or

$R^2$  has the formula:



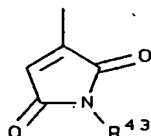
wherein:

- j is an integer from 0 to 8; and  
130 m is 0 or 1; and  
 $R^{30}$  and  $R^{31}$  are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and  
135  $R^{32}$  is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;  
140  $R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ , wherein  $R^{35}$ ,

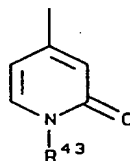
$R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

145  $R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or  $R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and

$R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,



; and



150

(IV)

(V)

wherein  $R^{43}$  is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

155 wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, 160 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, 165 alkoxy carbonyl, aryloxy carbonyl, heterocyclylalkoxy carbonyl, alkoxy carbonylamino, alkoxy aralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, heterocyclylalkylamino, aralkylheterocyclylamino, nitro, alkylaminocarbonyl, 170 alkylcarbonylamino, halo sulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl,

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arylhydrazinyl, or  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and

175  $R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  $R^4$  is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, 180 alkylsulfinylalkylene, arylsulfinylalkylene, alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, 185 nitro, alkylamino, arylamino, alkylaminoalkylene, arylaminoalkylene, aminoalkylamino, and hydroxy; provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl ring containing a 2-hydroxy substituent and when  $R^1$  is hydrido; further provided  $R^2$  is selected from aryl, heterocyclyl, 190 unsubstituted cycloalkyl and cycloalkenyl when  $R^4$  is hydrido; and further provided  $R^4$  is not methylsulfonylphenyl; or

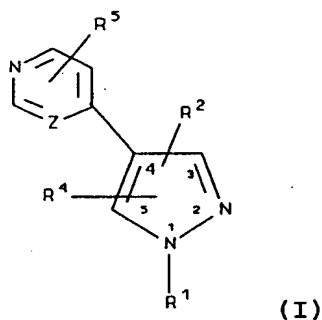
a pharmaceutically-acceptable salt or tautomer thereof.

116. A method of treating a p38 kinase mediated disorder, said method comprising treating the subject having or susceptible to such disorder with a therapeutically-effective amount of a compound of

5 Formula I

**SUBSTITUTESHEET (RULE 26)**

806



(I)

wherein

Z represents a carbon atom or a nitrogen atom; and

R<sup>1</sup> is selected from hydrido, lower alkyl, lower  
10 hydroxyalkyl and lower alkynyl; and

R<sup>2</sup> is selected from hydrido and lower alkyl; and

R<sup>4</sup> is selected from phenyl and benzodioxolyl; wherein  
phenyl is optionally substituted with one or more halo  
radicals; and

15 R<sup>5</sup> is selected from hydrido, halo and  
alkylhydrazinyl; or

a pharmaceutically-acceptable salt or tautomer  
thereof.

117. The method of Claim 112 wherein the TNF  
mediated disorder is selected from the group of disorders  
consisting of bone resorption, graft vs. host reaction,  
atherosclerosis, arthritis, osteoarthritis, rheumatoid  
5 arthritis, gout, psoriasis, topical inflammatory disease  
state, adult respiratory distress syndrome, asthma,  
chronic pulmonary inflammatory disease, cardiac  
reperfusion injury, renal reperfusion injury, thrombus,  
glomerulonephritis, Crohn's disease, ulcerative colitis,  
10 inflammatory bowel disease and cachexia.

**SUBSTITUTE SHEET (RULE 26)**

118. The method of Claim 112 wherein the TNF mediated disorder is inflammation.

119. The method of Claim 112 wherein the TNF mediated disease is arthritis.

120. The method of Claim 112 wherein the TNF mediated disorder is asthma.

121. The method of claim 112 wherein the compound is 4-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]pyridine or a pharmaceutically-acceptable salt or a tautomer thereof.

122. The method of claim 112 wherein the compound is 1-[5-(4-chlorophenyl)-4-(4-pyridinyl)-1H-pyrazol-3-yl]-4-methylpiperazine or a pharmaceutically-acceptable salt or a tautomer thereof.

123. The method of Claim 113 wherein the disorder is a p38 $\alpha$  kinase mediated disorder.

124. The method of Claim 113 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid  
5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis,  
10 inflammatory bowel disease and cachexia.

125. The method of Claim 113 wherein the p38 kinase mediated disorder is inflammation.

126. The method of Claim 113 wherein the p38 kinase

mediated disorder is arthritis.

127. The method of Claim 113 wherein the p38 kinase mediated disorder is asthma.

128. The method of Claim 116 wherein the disorder is a p38 $\alpha$  kinase mediated disorder.

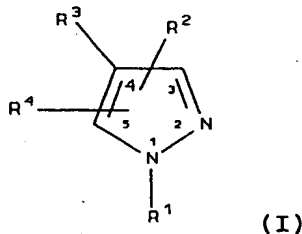
129. The method of Claim 116 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid  
5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis,  
10 inflammatory bowel disease and cachexia.

130. The method of Claim 116 wherein the p38 kinase mediated disorder is inflammation.

131. The method of Claim 116 wherein the p38 kinase mediated disorder is arthritis.

132. The method of Claim 116 wherein the p38 kinase mediated disorder is asthma.

133. A method of preparing pyrazoles of Formula I

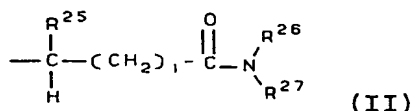




wherein

- $R^1$  is selected from hydrido, alkyl, cycloalkyl,  
 5 alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl,  
 cycloalkylalkylene, cycloalkenylalkylene,  
 heterocyclylalkylene, haloalkyl, haloalkenyl,  
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,  
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,  
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl,  
 heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl,  
 alkylthioalkylene, alkenylthioalkylene,  
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,  
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,  
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,  
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,  
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
 heterocyclylsulfonyl, alkylaminoalkylene,  
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,  
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,  
 heterocycliloxycarbonylalkylene, alkoxycarbonylarylene,  
 aryloxycarbonylarylene, heterocycliloxycarbonylarylene,  
 alkylcarbonylalkylene, arylcarbonylalkylene,  
 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 arylcarbonyloxyarylene, and  
 30 heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



wherein:

$i$  is an integer from 0 to 9;

- 35           R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene; and
- 40           R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and
- R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, 45 cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, 50 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxy carbonylarylene, 60 arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene, alkoxycarbonylalkoxylarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene, 65 aralkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, arylsulfonylaminoalkylene, alkylsulfonylarylene, alkylaminosulfonylarylene; wherein said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylheterocyclylarylene, 70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,

aryloxycarbonylarylene, arylcarbonylarylene, alkylthioarylene, heterocyclylthioarylene, arylthioalkylarylene, and alkylsulfonylarylene groups are optionally substituted with one or more radicals independently selected from alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano; or

75  $R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$  is selected from aralkyl, aralkoxyalkylene, heterocyclylalkylene, alkylheterocyclylalkylene, alkoxyalkyl, alkoxyalkylene, alkylthioalkylene, and aralkylthioalkylene; wherein said aralkyl and heterocyclyl groups are optionally substituted with one or more radicals independently selected from alkyl and nitro; or

80  $R^{26}$  and  $R^{27}$  together with the nitrogen atom to which they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocyclyl, heterocyclylalkylene, alkylheterocyclylalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxyalkyl, alkoxyalkylene, alkylamino and alkoxyalkylamino; wherein said aryl, heterocyclylalkylene and aryloxyalkylene radicals are

85 optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy; and

90  $R^2$  is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, heterocyclylalkylamino, aralkylamino, aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocycliloxy, alkylthio,

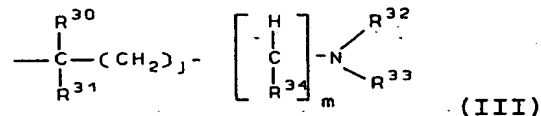
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arylthio, heterocyclylthio, carboxy, carboxyalkyl,  
 carboxycycloalkyl, carboxycycloalkenyl,  
 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,  
 110 alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl,  
 alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
 alkoxycarbonylaminoalkylamino, and heterocyclylsulfonyl;  
 wherein the aryl, heterocyclyl, heterocyclylalkyl,  
 cycloalkyl and cycloalkenyl groups are optionally  
 115 substituted with one or more radicals independently  
 selected from halo, keto, amino, alkyl, alkenyl, alkynyl,  
 aryl, heterocyclyl, aralkyl, heterocyclylalkyl,  
 epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy,  
 aralkoxy, haloalkyl, alkylamino, alkynylamino,  
 120 alkylaminoalkylamino, heterocyclylalkylamino,  
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,  
 arylsulfonyl, and aralkylsulfonyl; or

$R^2$  has the formula:



125 wherein:

$j$  is an integer from 0 to 8; and

$m$  is 0 or 1; and

$R^{30}$  and  $R^{31}$  are independently selected from hydrogen,  
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,  
 130 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,  
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and

$R^{32}$  is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 135 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 heterocyclylcarbonylaminoalkylene;

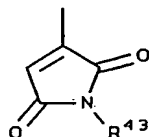
$R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  
 $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ , wherein  $R^{35}$ ,

SUBSTITUTE SHEET (RULE 26)

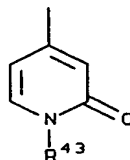
140  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

$R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

145  $R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and  $R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl,



; and



(IV)

(V)

150 wherein  $R^{43}$  is selected from hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

155 wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl and purinyl groups are optionally substituted with one or more radicals independently selected from halo, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, 160 cycloalkenylamino, arylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxycarbonyl, aryloxycarbonyl, heterocyclylalkoxycarbonyl, alkoxycarbonylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, 165 aralkylamino, heterocyclylalkylamino, aralkylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl,

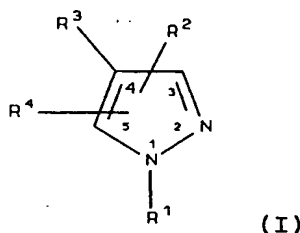
- 170 arylhydrazinyl, or  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and
- $R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  $R^4$  is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl,
- 175 alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene, alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
- 180 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene, arylaminoalkylene, aminoalkylamino, and hydroxy; or
- a pharmaceutically-acceptable salt or tautomer
- 185 thereof,
- said method comprising the steps of forming an acyl hydrazone and condensing to form the substituted pyrazole.

134. The process of Claim 133 wherein the acyl hydrazone is formed by reaction of a ketone with an acyl hydrazide.

135. The process of Claim 133 wherein the condensation is performed at a temperature from about 25 °C to about 200 °C.

136. A method of preparing pyrazoles of Formula I

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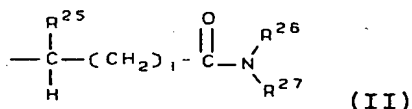
wherein

$R^1$  is selected from hydrido, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxy carbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocycliloxy carbonylalkylene, alkoxy carbonylarylene, aryloxy carbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and

**SUBSTITUTE SHEET (RULE 26)**

30 heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



wherein:

```
i is an integer from 0 to 9;
```

35 R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclalkylcarbonylaminoalkylene; and

40 R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxy carbonylalkylene, and alkylaminoalkyl; and

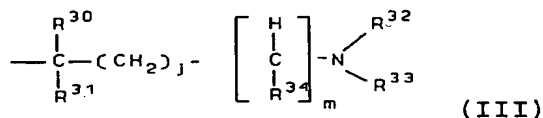
R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxy carbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene,



- alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
cycloalkylthioalkylene, alkylthioarylene,  
65 aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
heterocyclylalkylene, alkylheterocyclylarylene,  
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
are optionally substituted with one or more radicals  
75 independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
 $R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
80 alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups are optionally substituted with one  
or more radicals independently selected from alkyl and  
nitro; or  
85  $R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
90 alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
heterocyclylalkylene and aryloxyalkylene radicals are  
95 optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is selected from hydrido, halogen, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, heterocyclylalkylamino, aralkylamino, aminoalkyl, aminoaryl, aminoalkylamino, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, cycloalkyl, cycloalkenyl, alkoxy, heterocycliloxy, alkylthio, arylthio, heterocyclylthio, carboxy, carboxyalkyl, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonyl, alkoxylalkylamino, alkoxycarbonylaminoalkylamino, and heterocyclylsulfonyl; wherein the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and cycloalkenyl groups are optionally substituted with one or more radicals independently selected from halo, keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkyl, epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclylalkylamino, alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl, arylsulfonyl, and aralkylsulfonyl; or

$R^2$  has the formula:



wherein:

$j$  is an integer from 0 to 8; and

$m$  is 0 or 1; and

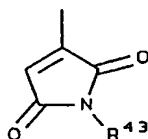
$R^{30}$  and  $R^{31}$  are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,

130 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,  
alkoxyalkyl, and alkylcarbonyloxyalkyl; and

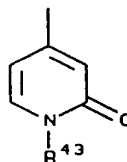
$R^{32}$  is selected from hydrogen, alkyl, aralkyl,  
heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
135 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
alkylcarbonylalkylene, arylcarbonylalkylene, and  
heterocyclylcarbonylaminoalkylene;

$R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  
 $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ , wherein  $R^{35}$ ,  
 $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently selected from  
140 hydrocarbon, heterosubstituted hydrocarbon and  
heterocyclyl; and

$R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl,  
alkylaminocarbonyl, and arylaminocarbonyl; or  
 $R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and  
145  $R^3$  is selected from pyridinyl, pyrimidinyl,  
quinolinyl, purinyl,



; and



(IV)

(V)

wherein  $R^{43}$  is selected from hydrogen, alkyl,  
150 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;  
and

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl and  
purinyl groups are optionally substituted with one or  
more radicals independently selected from halo, alkyl,  
155 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
alkenylamino, alkynylamino, cycloalkylamino,

- 160 cycloalkenylamino, arylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxy carbonyl, aryloxy carbonyl, heterocyclyl alkoxy carbonyl, alkoxy carbonylamino, alkoxy aralkylamino, aminosulfinyl, aminosulfonyl, alkylaminoalkylamino, hydroxyalkylamino, 165 aralkylamino, heterocyclylalkylamino, aralkylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, halosulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, or -NR<sup>44</sup>R<sup>45</sup> wherein R<sup>44</sup> is alkylcarbonyl or 170 amino, and R<sup>45</sup> is alkyl or aralkyl; and
- R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R<sup>4</sup> is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, 175 alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene, alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, 180 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxy carbonyl, aryloxy carbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene, arylaminoalkylene, aminoalkylamino, and hydroxy; or a pharmaceutically-acceptable salt or tautomer.
- 185 thereof,
- said method comprising the steps of treating a substituted ketone with an acyl hydrazide to give the pyrazole.

137. The process of Claim 136 wherein it is carried out in an acidic solvent.

138. The process of Claim 137 wherein the acidic solvent is acetic acid.

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139. The process of Claim 137 wherein the acidic solvent is an organic solvent containing an acid.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 98/10436

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D401/04 A61K31/415 A61K31/44 A61K31/505 C07D401/14  
C07D409/14 C07D413/14 C07D405/14 C07D471/04 C07D417/14  
C07D453/02 //(C07D471/04,237:00,231:00),(C07D471/04,237:00,

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 03385 A (SEARLE & CO ; LEE LEN F (US); PENNING THOMAS D (US); KRAMER STEVEN) 8 February 1996 cited in the application see abstract; claims 1,8,10 see page 10 - page 13 see page 17 see page 24 - page 26 see page 41 - page 44 ----	1-139
X	US 5 559 137 A (ADAMS JERRY L ET AL) 24 September 1996 cited in the application see abstract; claim 1; example 1 ----- -/-	1-139

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- "&" document member of the same patent family

Date of the actual completion of the international search

11 September 1998

Date of mailing of the international search report

24/09/1998

Name and mailing address of the ISA

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Authorized officer

Paisdor, B

# INTERNATIONAL SEARCH REPORT

In tional Application No

PCT/US 98/10436

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 233:00)

According to International Patent Classification(IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CATIVIELA C ET AL: "On the synthesis of 3(5)-(carbomethoxy)-4-hetarylpyrazoles" J. HETEROCYCL. CHEM. (JHTCAD,0022152X);88; VOL.25 (3); PP.851-5, XP002077334 Univ. Zaragoza;Inst. Cienc. Mater. Aragon; Zaragoza; 50009; Spain (ES) see page 851; examples 3E,3F,4E,4F see page 854	1-3, 9-11,15, 16,20,21
X	---	88-95
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

11 September 1998

Date of mailing of the international search report

Name and mailing address of the ISA  
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# INTERNATIONAL SEARCH REPORT

Int l tional Application No  
PCT/US 98/10436

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FISCHER U ET AL: "1,3-Dipolar additions to 7-methylthieno'2,3-c!pyridine 1,1-dioxide" HELV. CHIM. ACTA (HCACAV,0018019X);80; VOL.63 (6); PP.1719-27, XP002077335 F. Hoffmann-La Roche und Co., A.-G.; Pharm. Forschungsabt.; Basel; CH-4002; Switz. see page 1719; example 4 see page 1720; examples 10,13 see page 1721; examples 16,17,19,20	1-5, 9-11, 15-22
X	-----	88-95
A	CHEMICAL ABSTRACTS, vol. 098, no. 1, 3 January 1983 Columbus, Ohio, US; abstract no. 004498, POPOVA A N ET AL: "Synthesis of 4-(pyrazol-4-yl)-substituted salts of pyrylium and pyridines" XP002077337 see abstract	1-3, 9-11,15, 16,20,21
X	& KHIM. GETEROTSIKL. SOEDIN. (KGSSAQ,04538234);82; (9); PP.1280, Rostov. Gos. Univ.;Rostov-on-Don; 344006; USSR (SU)	88-95
A	BAUER V J ET AL: "4-'3(5)-Pyrazolyl!pyridinium salts. A new class of hypoglycemic agents" J. MED. CHEM. (JMCMAR);68; VOL.11 (5); PP.981-4, XP002077336 Div. of Amer. Cyanamid Co.;Lederle Lab.; Pearl River; N. Y. see page 981; examples 1-5 see page 982; table I see page 983; table II	1-3, 9-11,15, 16,20,21
X	-----	88-95



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 10436

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 112-132  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 112-132  
are directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

In International Application No

PCT/US 98/10436

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9603385 A	08-02-1996	US 5486534 A	23-01-1996
		AU 3126795 A	22-02-1996
		CA 2195123 A	08-02-1996
		EP 0772597 A	14-05-1997
		JP 10503201 T	24-03-1998
		US 5580985 A	03-12-1996
		US 5756530 A	26-05-1998
US 5559137 A	24-09-1996	JP 10500413 T	13-01-1998
		WO 9531451 A	23-11-1995